INTRODUCTION

Adenocarcinoma of stomach was the leading cause of cancer related mortality worldwide among the 20th century. It is only the second most common cause of cancer related mortality next to lung cancer. So it is called as 'CAPTAIN OF MEN OF DEATH'.

The mainstay of treatment is surgical resection for adenocarcinoma stomach.But the overall survival and also the resectability of the tumor depends upon the lymphovascular spread, adjacent spread and distant metastasis to other vital organs.

The metastasis of the tumor are identified by various means, especially for adenocarcinoma stomach by upper gastrointestinal endoscopy, ultrasonogram of abdomen, contrast enhanced computed tomography of the abdomen. All of these shows the metastasized lesions in various parts of the body.

There were some associations studied between the coagulation factors and gastrointestinal malignancies the first one has been documented around 1865. It has been suggested that the thrombin has been a potent promoter along with fibrin for the formation of a protective shield around the tumor emboli in the circulation there by preventing them being attacked by the immunocompetent cells in the circulation, there by augmenting their metastasis for both lymphovascular invasion and distant metastasis. In addition there has been a

view suggesting that the coagulation factors in plasma augments the tumor growth, it's angiogenesis and thereby its progression.

So, the haemostatic factors especially the prothrombin time and nodal metastasis in gastric cancer cases have been compared in this study as the prothrombin time is found to be more in correlation with the lymphovascular invasion than other haemostatic factors in other studies conducted.

AIMS AND OBJECTIVES OF THIS STUDY

1. TO KNOW THE DISREGULATION OF PROTHROMBIN TIME IN CASES OF OPERABLE GASTRIC CANCER

2. TO STUDY THE CORRELATION BETWEEN ELEVATION OF PROTHROMBIN TIME AND NODAL METASTASIS IN OPERABLE CASES OF GASTRIC CANCER.

REVIEW OF LITERATURE

HISTORY OF GASTRIC CANCER:

The history of gastric cancer dated back to 1600BC according to eber papyrus and also in the reports of Hippocrates around the second century AD. Around the 980 AD, Avicenna of Arabia, in his encyclopedia had mentioned about the adenocarcinoma of stomach. After that there was no remarkable development in the knowledge about gastric carcinoma except for the purgatives and blood letting concept according to the black bile theory of Hippocratic period, till in 1835, two types of gastric ulcer defined as malignant and benign by Cruvelhier

GASTRIC CARCINOMA AND THE GREAT NAPOLEAN BONAPARTE:

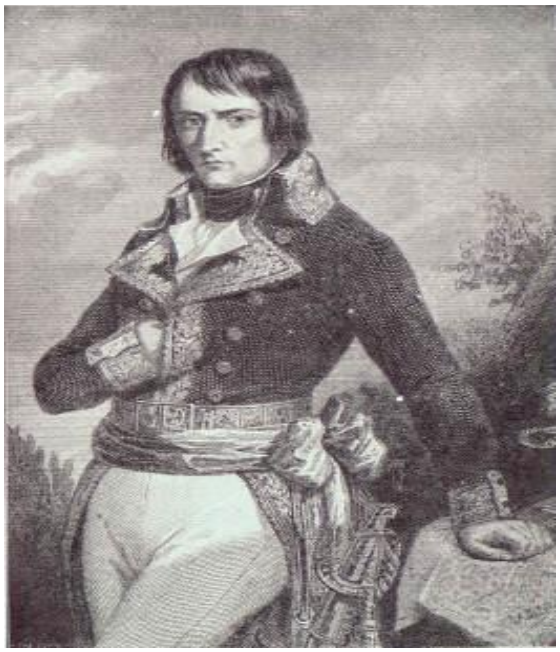
History says that the French emperor Napoleon Bonaparte could have suffered from a schirrous form of carcinoma of the stomach following a familial history as reported by his family physician, Dr.Antonmarchi. He exiled to St.Helena, an island in the Atlantic Ocean, after following a defeat in the war of waterloo.

During his St.Helena exile, In 1819 he had suffered from repeated episodes of abdominal pain, fever, vomiting especially of blood and also had severe hiccoughs. He was treated with large doses of purgatives and blood letting following this treatment his symptoms worsened around September 1820, he

was suffered from vomiting daily and with altered bowel habits, epigastric pain, fatigue and fever

In 1821, he had vomited coffee-ground coloured vomitus and had severe hiccoughs and tachycardia and also had delirium. Following this he told Dr.Antonmarchi, as follows ". . . I desire you operate me and examine my stomach and then make a detailed report of it and you should give to my son." He knew that he had been suffering from a gastric problem as his father and family relatives also shared the similar illness in their last days of life. In 1821, may 5, in the early morning following a bout of haemetemesis and melena he died of hypovolemic shock

FIG:THE NAPOLEAN BONAPARTE AND HIS EPIGASTRIC PAIN.



Eight physicians attended the autopsy of Napoleon Bonaparte. Of them except Dr.Francesco Antonmarchi who was his friend and family physician, other seven were british. The more detailed report after attending the autopsy by Antonmarchi, who was an anatomopathologist of university of Pisa as follows:

". . . the gastric volume was smaller, it's anterior surface is normal and on the right side there is a close adhesion with the inferior and perforated in the center. The perforation was sealed by the liver adhesion. On opening the stomach, over the Greater curvature it's capacity appeared filled with a coffee coloured liquid. The interior of the stomach was a cancerous ulcer whose center was near the lesser curve and the induration spread from the cardiac to pylorus, with a scirrhous thickening of the wall."

During that times as the microscopical examination of the tissues was not developed the diagnosis made from from autopsy mainly relied upon the morphological analysis of the tissues. So, the reports clearly indicates that the Napoleon Bonaparte had schirrous gastric carcinoma probably with gastric outlet obstruction which had manifested in the later stages as intractable vomiting and hiccoughs. Previously , the emperor had suffered from vague abdominal symptoms, perhaps due to chronic gastritis which preceded his familial gastric cancer for many years

In the year 1874-76, Billroth was the first one to describe the distal gastric resection along with anastamosis of the stomach and to duodenum so called the

Billroth type 1, then resection of the stomach and then anastamosis to the proximal jejunum so called the Billroth type 2. In 1879, Pean was the first to do a gastric resection for malignancy, but the patient died on his fifth postoperative day.

In 1881, Billroth did his first successful gastric resection. In the same year, Wolfer & Nicolodani did the antecolic gastrojejunostomy. In 1883, Courvoisier did the retrocolic gastrojejunostomy. In 1893, he also advised the jejunojejunostomy with the gastrojejunostomy. In 1898, Schlatter for the first time in history performed the total gastrectomy for malignancy. In 1907, Wendel performed the first oesophagogastrectomy for proximal gastric cancer.

In 1930, Polya performed the anastamosis of entire opening of the stomach with the jejunum

In 1981, Longmire performed the first radical resection for gastric cancer. Later then immense progress has been achieved in the field of radical as well as curative resection for the carcinoma stomach. The recent standard of surgery now remains as the main stay of resection for carcinoma stomach is the total/subtotal gastrectomy followed by D2 lymphadenectomy which in addition to the stomach includes all the per igastric nodal basins the initial sites of lymphovascular invasion.

In 1982, Robin warren and Barry marshall found that the H.pylori was responsible for benign and malignant lesions of the gastric mucosa especially in the endemic areas. In 1978, Stanley cohen discovered that the epidermal growth factor was found in the gastrectomy specimens for carcinoma stomach.

Earlier in history correlation between the coagulation factors and the metastatic emboli formation and its survival in the circulation has been studied which was evident in the routine investigations. There by the micrometastasis which requires the protective plug around it formed by the coagulation factors can be interrupted by the utilization of the anticoagulants which also proved by some studiesaround the world.

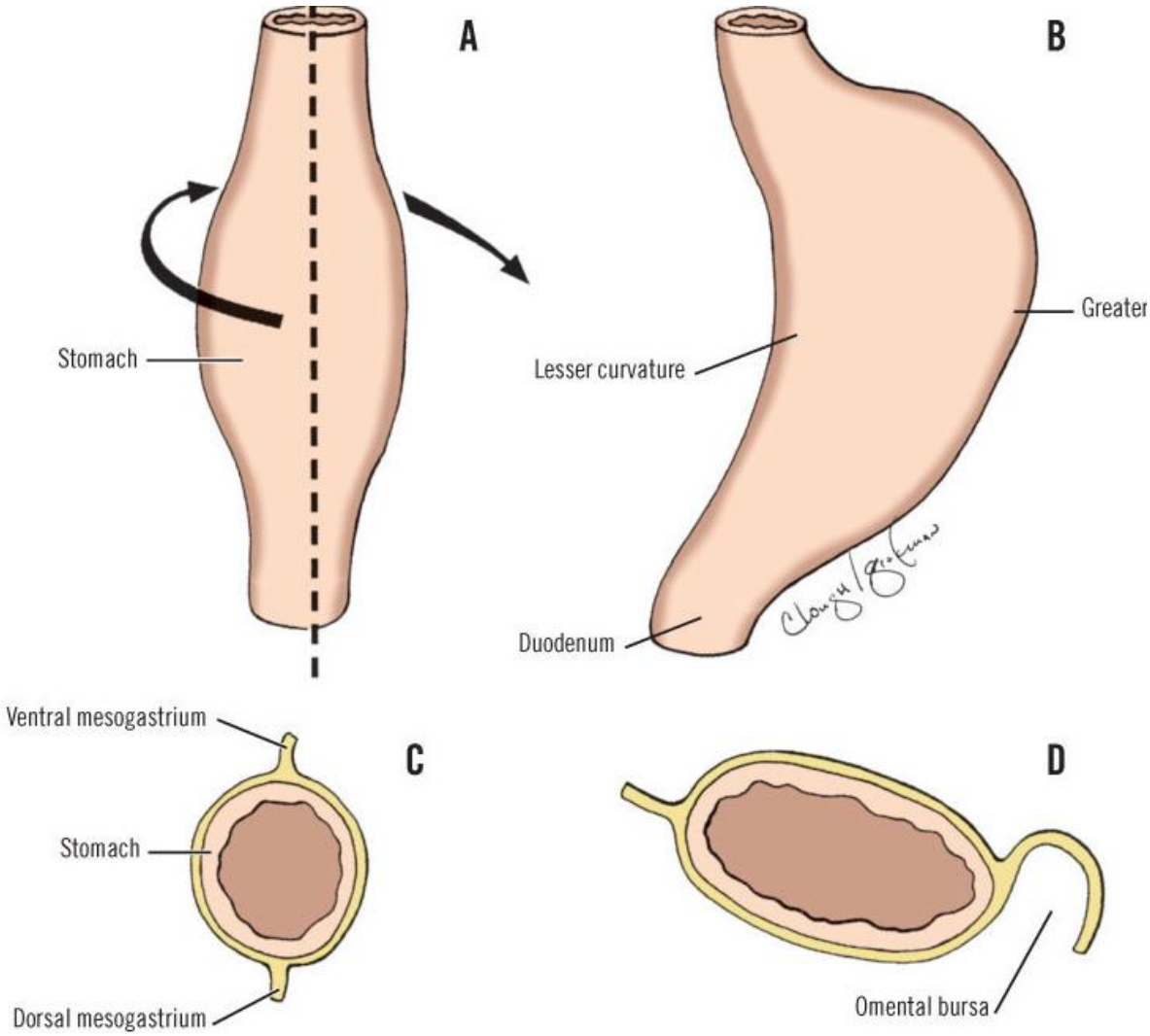
EMBRYOLOGY OF STOMACH:

The primitive form of the esophagus, stomach, and proximal duodenum are formed by the elongation of the embryonic foregut. During the 4^{th} or 5^{th} week of gestation dilatation starts at the level of C3-C5. At the end of the seventh week the stomach may be found at T5-T10 by the cephalad growth of the surrounding torso. The truncal growth causes the stomach to locate between T10 and L3, its normal final position around the 10^{th} week

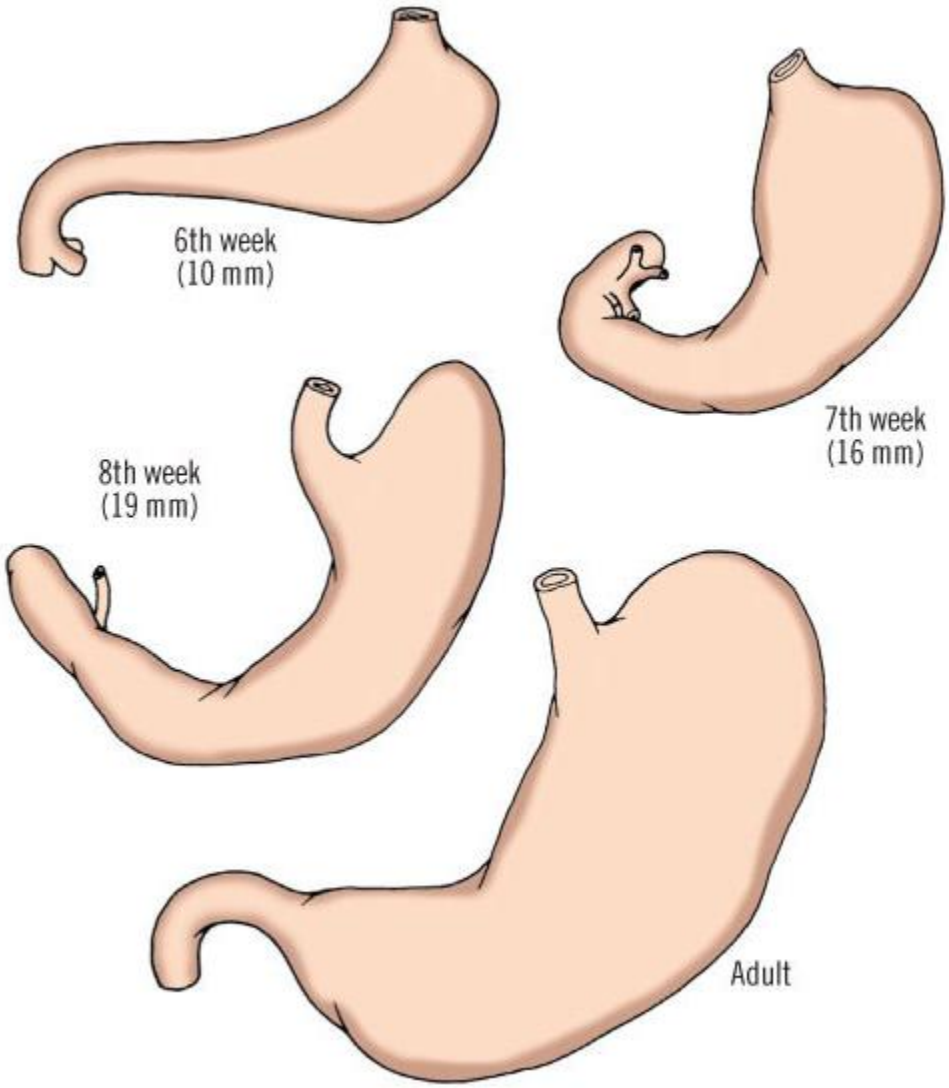
A 90° clockwise rotation takes place around the longitudinal axis of the stomach, making the dorsal mesogastrium to occupy the left side and ventral one to occupy the right side with formation of the omental bursa. Because of

this rotation the left vagal trunk innervates the anterior gastric wall and the right trunk innervates the posterior gastric wall.

The anteroposterior axis rotation also takes place with changes in the position of the gastric cardia and fundus, and so the position of the pylorus and gastroduodenal junction. Therefore, the dorsal surface of stomach becomes the greater curvature and the ventral surface becomes the lesser curvature of the stomach. At the fourth month of gestation the concavity of the lesser curvature of stomach and, at the eighth month, the fundic outgrowth of the stomach are two notable changes that occurs due to the slow growth of the lesser curvature compared to that of the greater curvature.



The above picture depicts the elongation of foregut and further rotational changes as described above

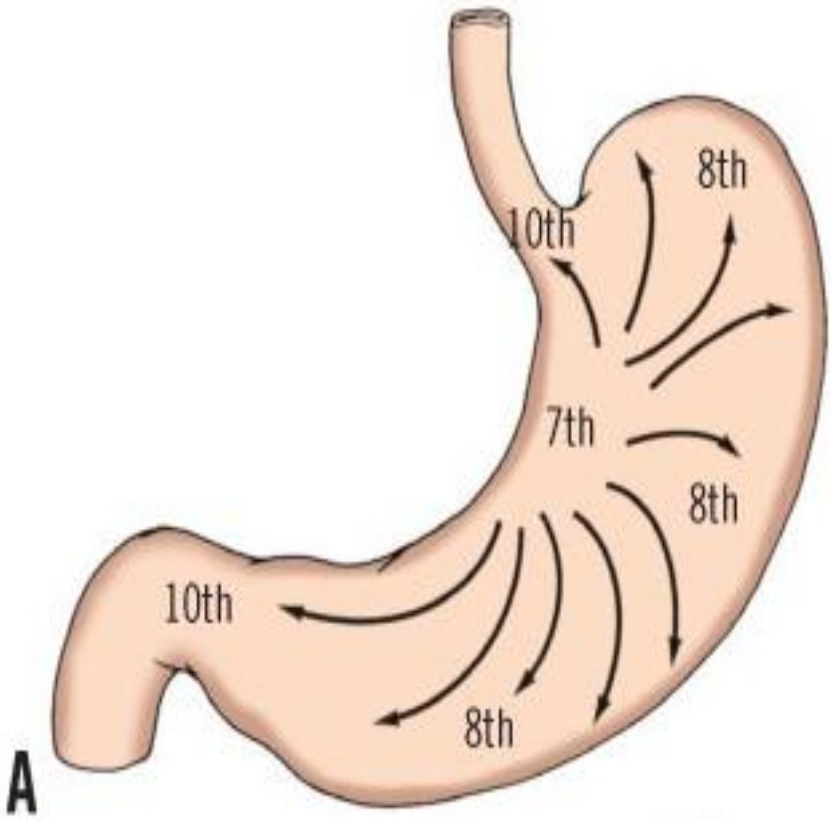


The above picture depicts the disproportionate growth of the lesser and greater curvatures of the stomach.

The gastric rugae makes it's appearance in the 8^{th} week of gestation. The muscularis emerges between the 8^{th} & 14^{th} weeks of gestation. The glandular pits first occur at the lesser curvature around 8^{th} week and by 10^{th} week they

spread throughout the stomach. Parietal cells are found in the gastric mucosa by 11^{th} week

The chief cells are found in the 12^{th} week of gestation. Pepsin is found to be present in the mucosa by last half of the sixth month.



The picture depicts the appearance of the gastric rugae in stomach.

ANATOMY OF STOMACH:

The stomach is the proximal most abdominal organ of the gastrointestinal tract, recognized as a pear shaped organ. The stomach is divided into four regions by arbitrary lines.

The region of the stomach that is contact with the esophagus is called the cardia. Just prior to beginning of the cardia of the stomach is the physiologically competent lower esophageal sphincter.

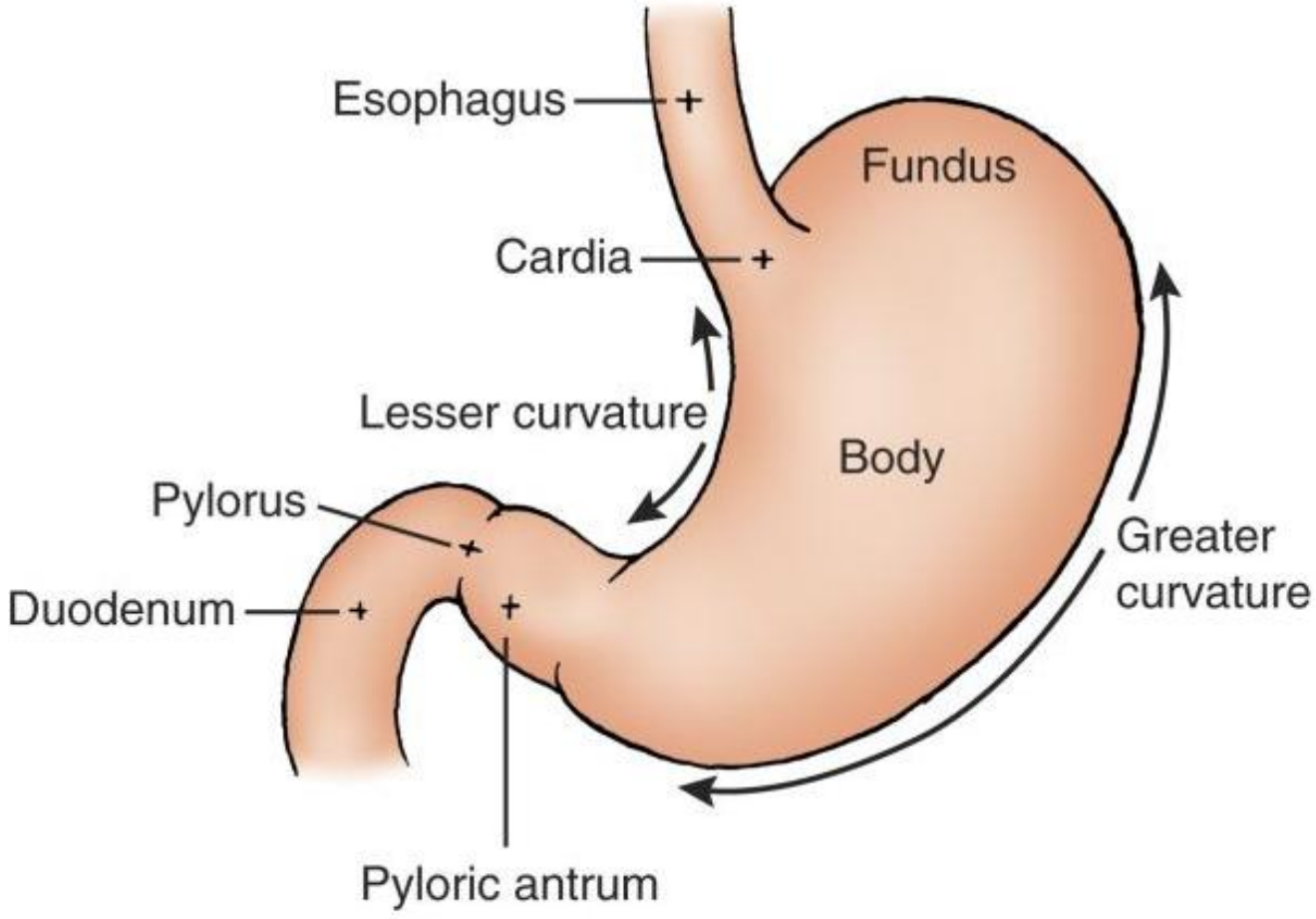
The pylorus of the stomach connects the distal stomach and the 1st part of the duodenum. The stomach is has been fixed at two points, the gastroesophageal junction and at the pyloric region, but the large midportion is mobile in nature.

The proximal part of the stomach is the floppy and distensible called as fundus. It is bounded by the diaphragm and the spleen superiorly and laterally respectively.

The rest of the stomach is called as the body of the stomach. It contains the bulk of the gastric parietal cells. On the right of the body of the stomach there is a concave lesser curvature and the convex greater curvature on the left of it.

At the incisura angularis, the lesser curvature angles to the right at an acute angle. This marks the end of the body of the stomach and the start of the antrum, which extends upto the pylorus.

Angle of His is one of the important anatomic landmark, formed by the fundus of the stomach with left lower end of oesophagus.



The figure depicts the divisions of stomach.

ANATOMIC RELATIONSHIPS OF THE STOMACH:

Most of the portion of the stomach lies in the left hypochondrial quadrant of the abdomen. Normally the gastroesophageal junction is around 2 to 3 cm below the diaphragmatic esophageal hiatus in the horizontal plane of the 7th chondrosternal junction, a plane slightly above the pyloric plane. The left lobe of the liver anteriorly covers a major portion of the stomach. The rest of the stomach is bounded by thoracic wall, diaphragm, and abdominal wall.

The anatomic relationships of the stomach to the adjacent intra-abdominal organs has important role in the manifestations and management of the disease. Adjacent organs which lie dorsal and ventral, are the pancreas and liver respectively, as well as the spleen lies immediately to the left of the greater curvature of the stomach. The transverse colon lies caudal to the stomach and may get obstructed as a result of neoplastic invasion or from peptic ulceration. The biliary structures lies along the free slip of the hepatoduodenal ligament and descends posterior to the 1st part of the duodenum and may get injured during gastrectomy.

Ligamentous attachments of the stomach are responsible for the positioning of it in the abdominal cavity.

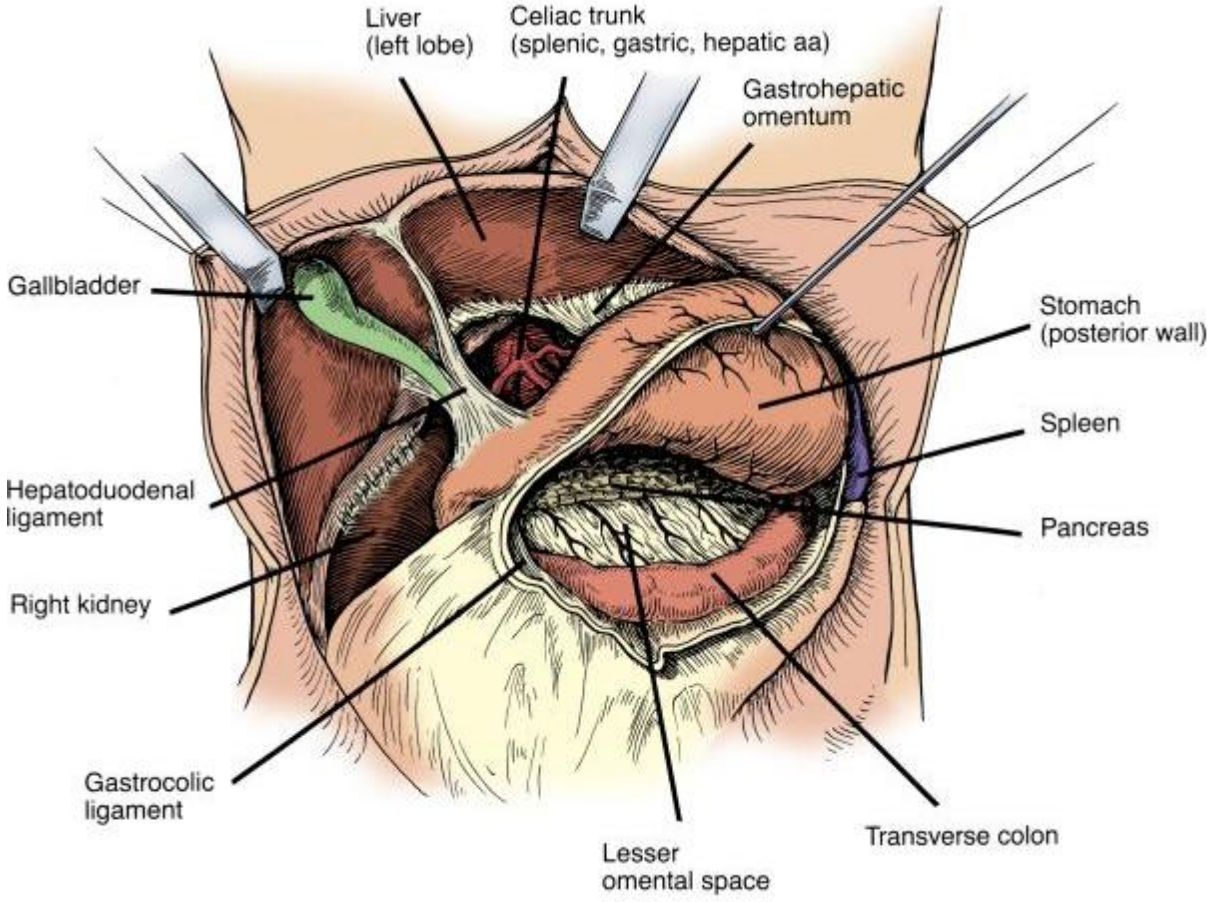
The gastrocolic ligament attaches the greater curvature of the stomach and the transverse colon and runs along with the greater omentum forming a

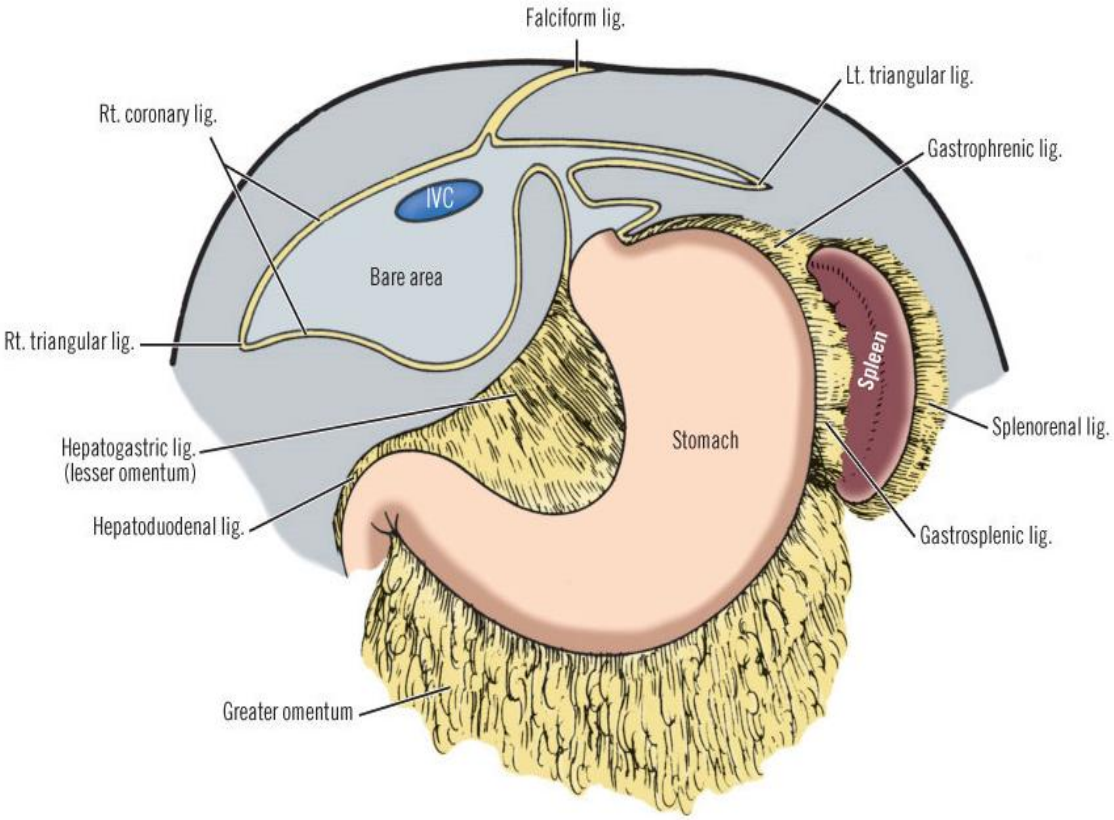
layer of it, which fans out freely in the peritoneal cavity from the transverse colon.

The lesser omentum is a double layered peritoneum extending from the porta hepatis of the liver extending upto the lesser curvature of the stomach and to the 1st part of the duodenum. The lesser omentum forms the anterior wall of the lesser sac and made up of the hepatogastric and hepatoduodenal ligaments.

The lesser omentum in it contains the left and right gastric vessels and along its right free margin contains three portal triad structures- the hepatic artery, bile duct, and portal vein. The hepatogastric ligament attaches the stomach's lesser curvature to the liver.

The gastrosplenic ligament extends from the greater curvature of the stomach to the hilum of the spleen and contains the short gastric vessels and the left gastroepiploic vessels. The gastrophrenic ligament runs from the upper portion of the greater curvature of the stomach to the diaphragm.


Liver
(left lobe)
Celiac trunk
(splenic, gastric, hepatic aa)
Gastrohepatic
omentum
Gallbladder
Stomach
(posterior wall)
Spleen
Hepatoduodenal
ligament
Pancreas
Right kidney
Gastrocolic
ligament
Lesser
omental space
Transverse colon


Falciform lig.
Lt. triangular lig.
Rt. coronary lig.
Gastrophrenic lig.
IVC
Bare area
Rt. triangular lig.
Spleen
Splenorenal lig.
Stomach
Hepatogastric lig.
(lesser omentum)
Hepatoduodenal lig.
Gastrosplenic lig.
Greater omentum

BLOOD SUPPLY OF THE STOMACH:

The stomach derives the major portion of its arterial supply from the celiac axis through four arteries:

The left gastric artery is the largest artery is the largest artery supplying the stomach. It arises from the celiac axis and runs along the lesser curvature of the stomach to anastamose with the branches of the right gastric artery, sometimes it gives rise to aberrant left hepatic artery.

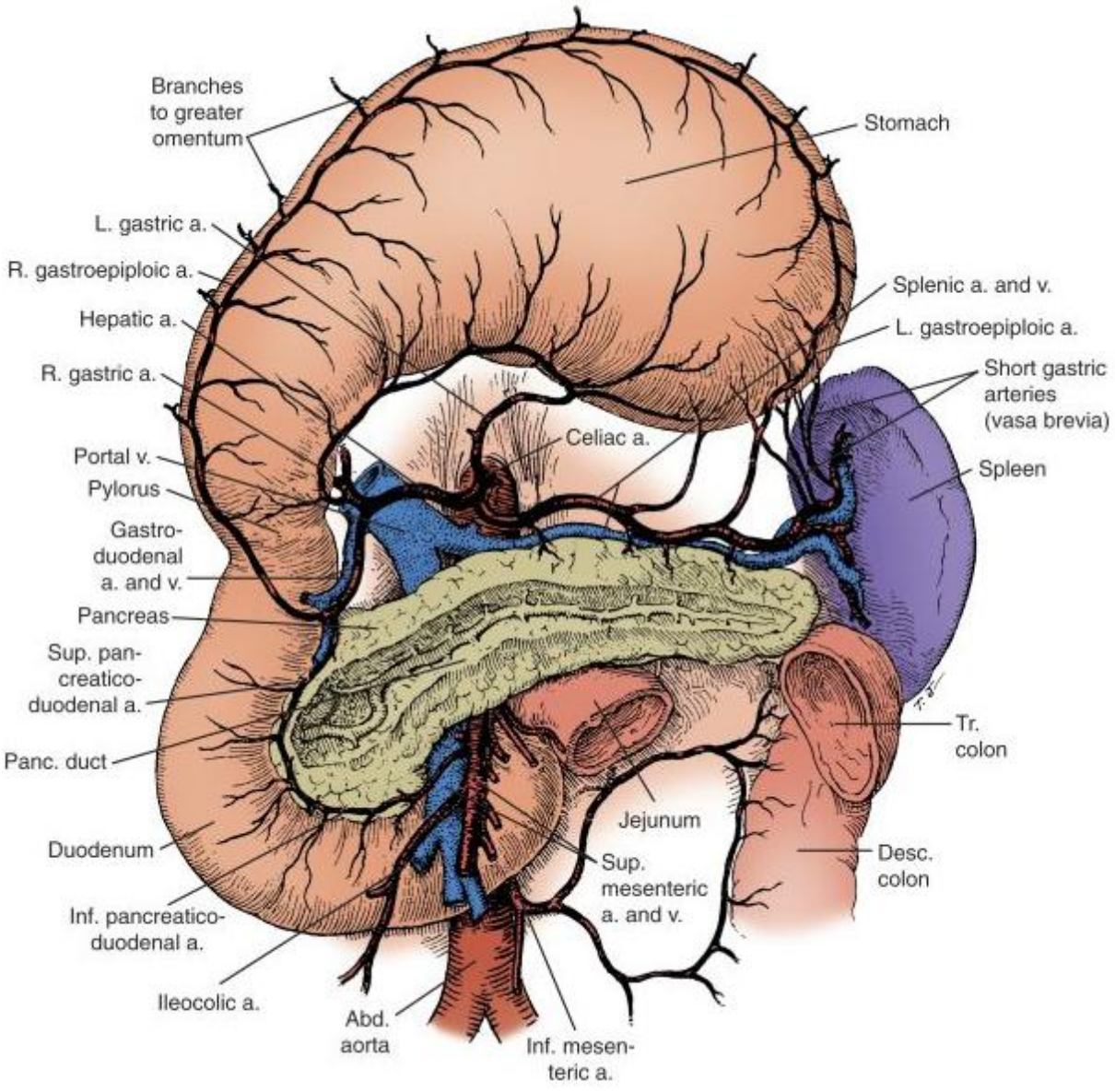
The right gastric artery is the branch of the hepatic artery runs along the lesser curvature and joins the left gastric artery.

The right gastroepiploic artery arises from the gastroduodenal artery just beyond the pyloric channel and ascends along the greater curvature of the stomach. The left gastroepiploic artery a branch of the splenic artery supplies the greater curvature of the stomach and descends down to anstamose with its companion the right gastroepiploic artery.

A small amount of blood supply to the proximal portion of the stomach is by the inferior phrenic arteries and also by the short gastric arteries branching from splenic artery.

Generally, the venous outflow of the stomach parallels the arterial vasculature of it. The portal vein drains the left gastric and the right gastric

veins from the stomach. The superior mesenteric vein drains the right gastroepiploic vein whereas the splenic vein drains the left gastroepiploic vein. Final pathway for all of this the portal vein.



LYMPHATIC SUPPLY OF THE STOMACH:

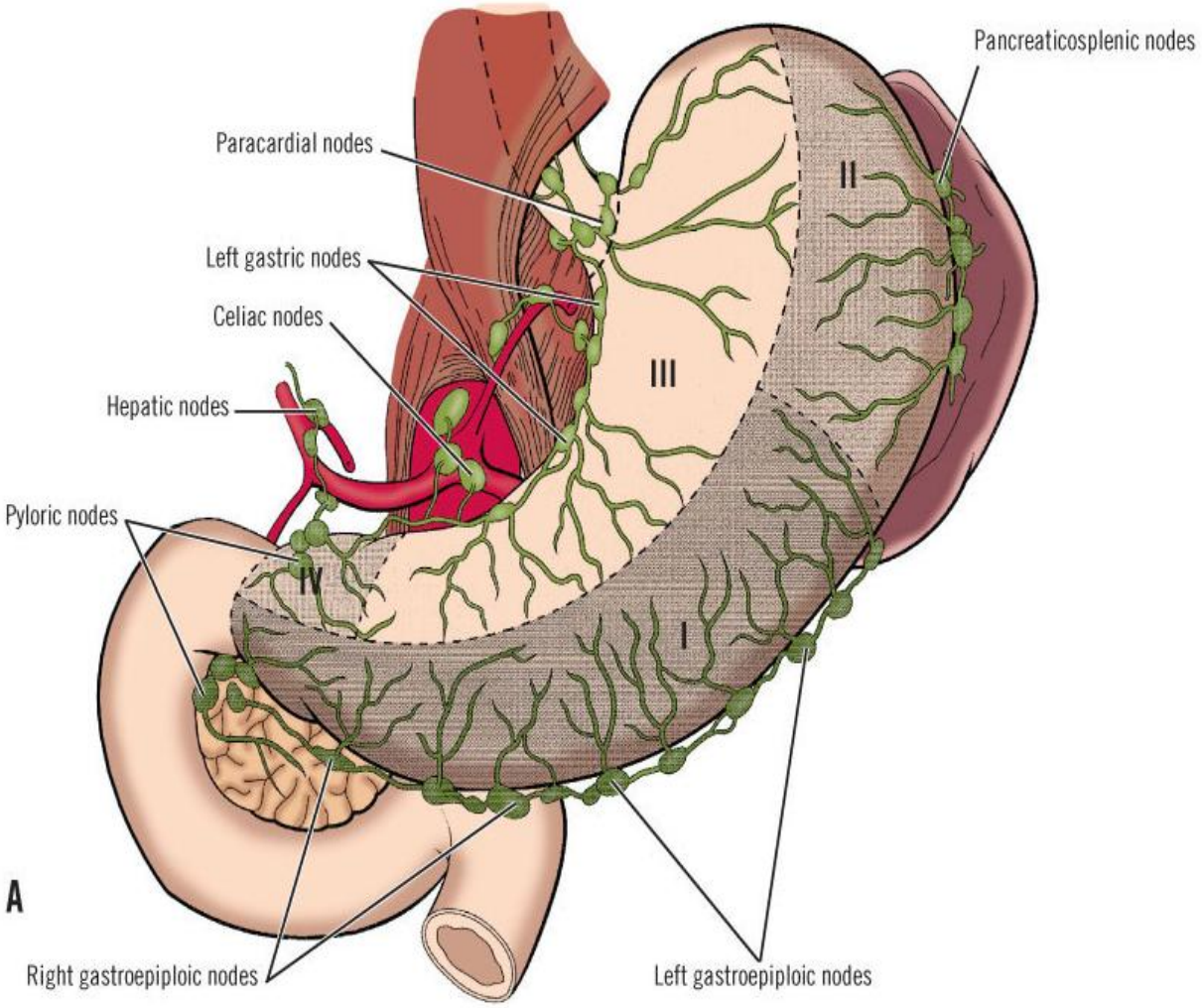
The lymphatic drainage like the venous outflow of stomach usually parallels the vasculature. The cardia and medial half of the body drain to the left

gastric nodes. The lesser curvature sides of the distal antrum and pylorus drain to the right gastric nodes.

The greater curvature half of the distal 60% of the stomach drains into the right gastroepiploic nodal chain, whereas the proximal greater curvature drains into the left gastroepiploic chain. These four groups of nodes all drain to the celiac group, from which lymph drains into the thoracic duct.

A gastric cancer anywhere in the stomach can metastasize to any of the perigastric nodal groups. The rich lymphatic plexus in the submucosal plane is responsible for microscopic appearance of tumor cells several centimeters away from the resection margin of gross disease.

The anatomy of the lymph drainage of the stomach has received renewed interest as reports suggest that there may be improved survival with extended lymph node dissection in patients undergoing gastrectomy for primary gastric cancer, although this comes at a cost of increased morbidity.



The above picture depicts the lymphatic supply of the stomach.

INNERVATIONS OF THE STOMACH:

The stomach has two modes of innervation both extrinsic and intrinsic. The extrinsic mode of innervation is mainly parasympathetic via vagus and sympathetic via the celiac plexus. The vagus nerve arises from it's nucleus in the floor of the 4th ventricle, it traverses the carotid sheath in the neck and in

the mediastinum, it divides into several branches. These branches unite just above the esophageal hiatus in the diapraghm to form the left and right vagus nerves.

At the GEJ, the left vagus trunk is anterior, and the right vagus trunk is posterior. Near the cardia, the left vagus trunk gives off a hepatic branch and then continues along the lesser curvature as the anterior nerve of Latarjet. The antral and pyloric portions of this nerve (crow's foot) must be preserved during a highly selective vagotomy so that gastric emptying is not compromised.

The “criminal” nerve of Grassi is the first branch of the right vagus nerve. This branch is a cause of recurrent gastric ulcers when left undivided during vagotomies. The right nerve gives a branch to the celiac plexus and then continues posterior to the stomach along the lesser curvature.

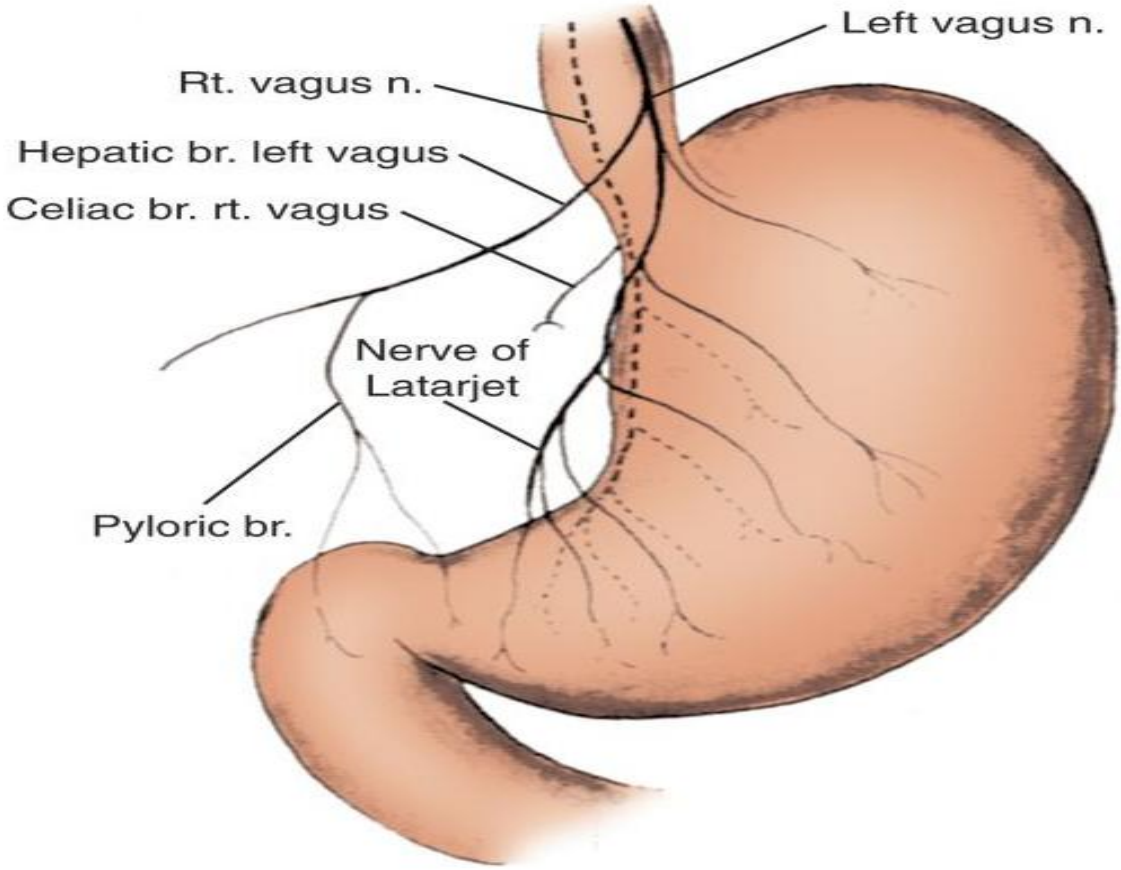
The most of the fibers of vagal nerve trunks are afferent in nature and they carry sensory stimuli from the gut to the brain. The efferent fibers of the same originate in dorsal nucleus of the medulla and these fibers synapse with neurons in the myenteric and submucosal plexuses.

Acetylcholine is the neurotransmitter of these neurons and they influence the gastric motor function and it’s secretion. The sympathetic nerve supply of stomach arises from T5-T10 level and travels through splanchnic

nerve to the celiac ganglion. Then the postganglionic fibers travel along with the arterial system to innervate the stomach.

The enteric nervous system of the stomach is composed of neurons in Auerbach's myenteric plexus located between the longitudinal and circular muscle layers and Meissner's submucosal plexus located between the muscularis mucosa and circular muscle autonomic plexuses.

Cholinergic, serotonergic, and peptidergic neurons are present in addition to a newly identified system of neurons that use a nonadrenergic noncholinergic (NANC) pathway. There are probably more neurons in the intrinsic gastric nervous system than there are gastric vagal efferent fibers.The function of these neurons is still poorly understood

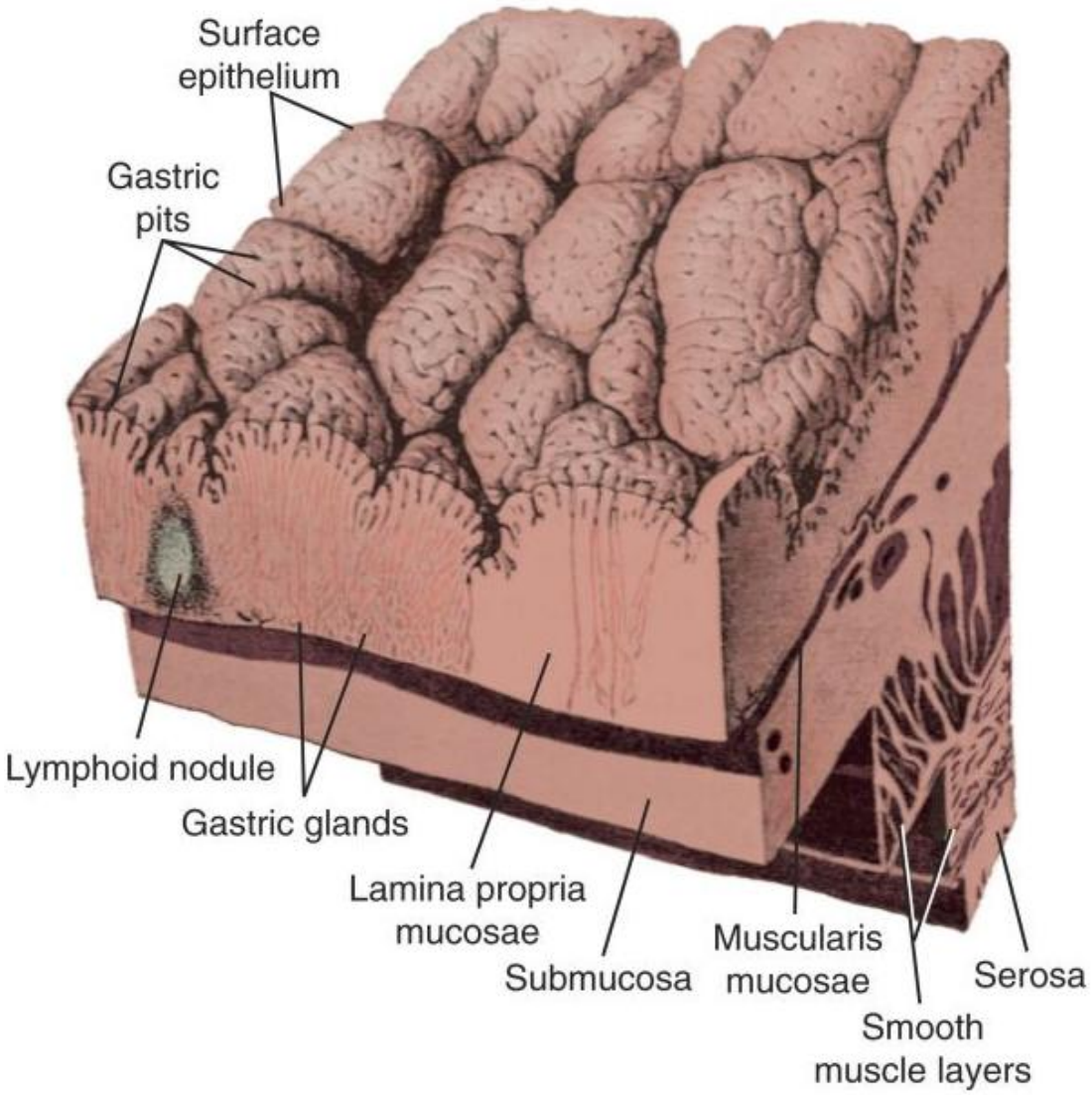


GASTRIC MORPHOLOGY:

The stomach is covered all around by peritoneum except for the exact lesser and greater curvatures and a small area on the posterior aspect at the proximal cardia and the distal pyloric antrum. The peritoneal coat forms the outer serosa. Below this is the thicker muscularis propria, which consists of three layers of smooth muscle. The middle layer of the muscularis propria is circular and is the only complete muscle layer. This layer becomes progressively thicker towards the pylorus, where it becomes impressively thick as a true sphincter located anatomically.

The outer most layer of muscularis propria is longitudinal and continuous with the outermost layer of longitudinal esophageal smooth muscle. Between the layers of muscularis externa is Auerbach's myenteric plexus. In between the layers of muscularis externa and the mucosa lies the submucosa, a collagen-rich layer of connective tissue that gives support to the stomach wall. The rich network of lymphatics and blood vessels described earlier lies in this layer, and it also contains Meissner's plexus.

The mucosa consists of three layers, they are surface epithelium, lamina propria, and muscularis mucosae. The muscularis mucosae lies on the inner aspect of the submucosa and it is responsible for the gastric rugae which greatly increases the epithelial surface area. It marks the microscopic discrimination of invasive and noninvasive gastric carcinoma. The lamina propria is a connective tissue layer that has the vessels, lymphatics, and nerves to support the surface epithelium of the stomach.



Gastric glandular organization:

The gastric mucosa consists of columnar epithelium with gastric glands. The functions and the cell types of the gastric glands vary according to their location in stomach. In the cardia, the gastric glands are arranged in a branched way that secretes mostly mucus. In the fundus and body of the stomach, the glands are more tubular. The fundus has an elaborate network of

glands that arise from the base of the mucosa in groups of four or five and join together at the bottom of the gastric pit, or foveola.

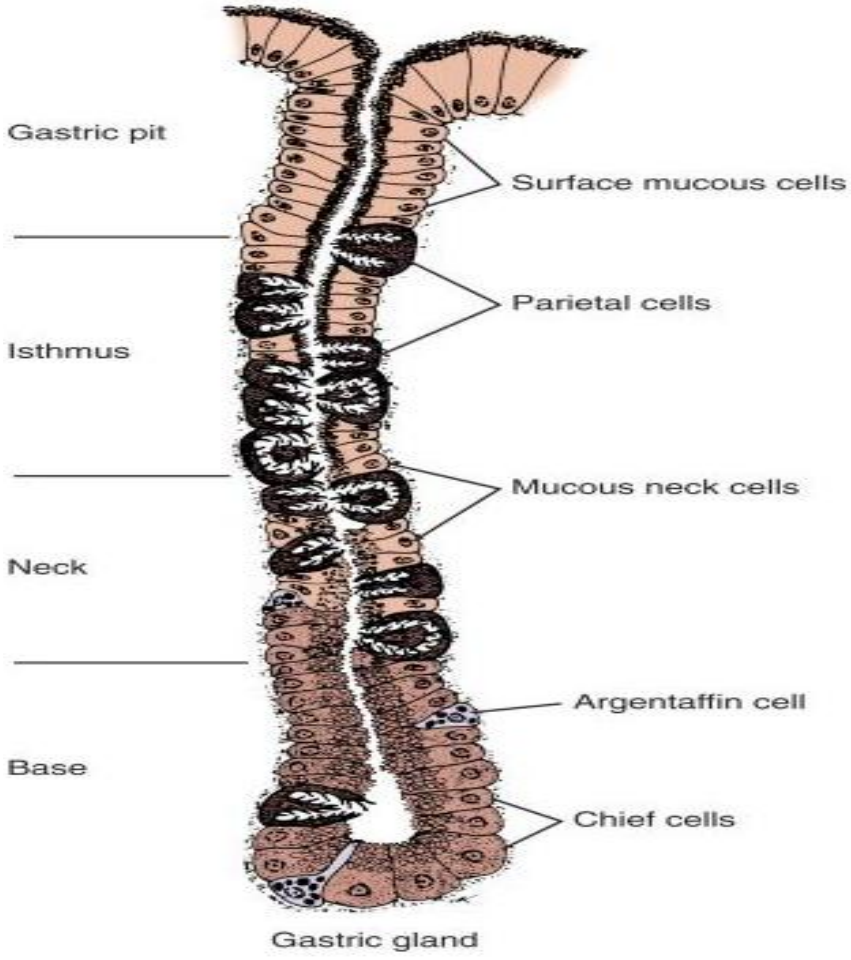
In the antrum of the stomach, the glands are again more branched and lined by mucus secreting surface epithelial cells on the luminal side that extend down into the necks of the glands.

The glands at the cardia are mostly mucus secreting in nature. In body of the stomach, the gastric glands are lined by parietal and chief cells. Only few parietal cells are seen in the fundus and proximal antrum.the parietal cells are absent in cardia and prepyloric region of stomach. Gastric mucosa have the following composition- 13% of parietal cells, 44% of chief cells, 40% of mucous cells, and 3% of endocrine cells.

Cells	**Location**	**Function**
Parietal	Body	Secretion of acid, ghrelin, leptin, and intrinsic factor
Mucus	Body, antrum	Mucus
Chief	Body	Pepsin and leptin
Surface epithelial	Diffuse	Mucus, bicarbonate, and prostaglandins
ECL	Body	Histamine
G	Antrum	Gastrin
D	Body, antrum	Somatostatin

Cells	Location	Function
Gastric mucosal interneurons	Body, antrum	Gastrin-releasing peptide
Enteric neurons	Diffuse	CGRP, others

CGRP, calcitonin gene–related peptide; ECL, enterochromaffin-like



GASTRIC PHYSIOLOGY:

Gastric mucosa is constantly in contact with secreted acid and foreign objects such as food. Hence most prone for injury either physical or chemical. It's being protected from the injuries by following mechanisms:

1.Increased blood flow helps in the rapid turnover of the epithelium and buffers the effect of acid in the lumen

2.Bicarbonate acts as a aci buffer

3.Mucus creates a barrier between contents and epithelium.

4.Augmentation blood flow to the mucosa by the prostaglandins

5.Bombesin increases prostaglandin secretion.

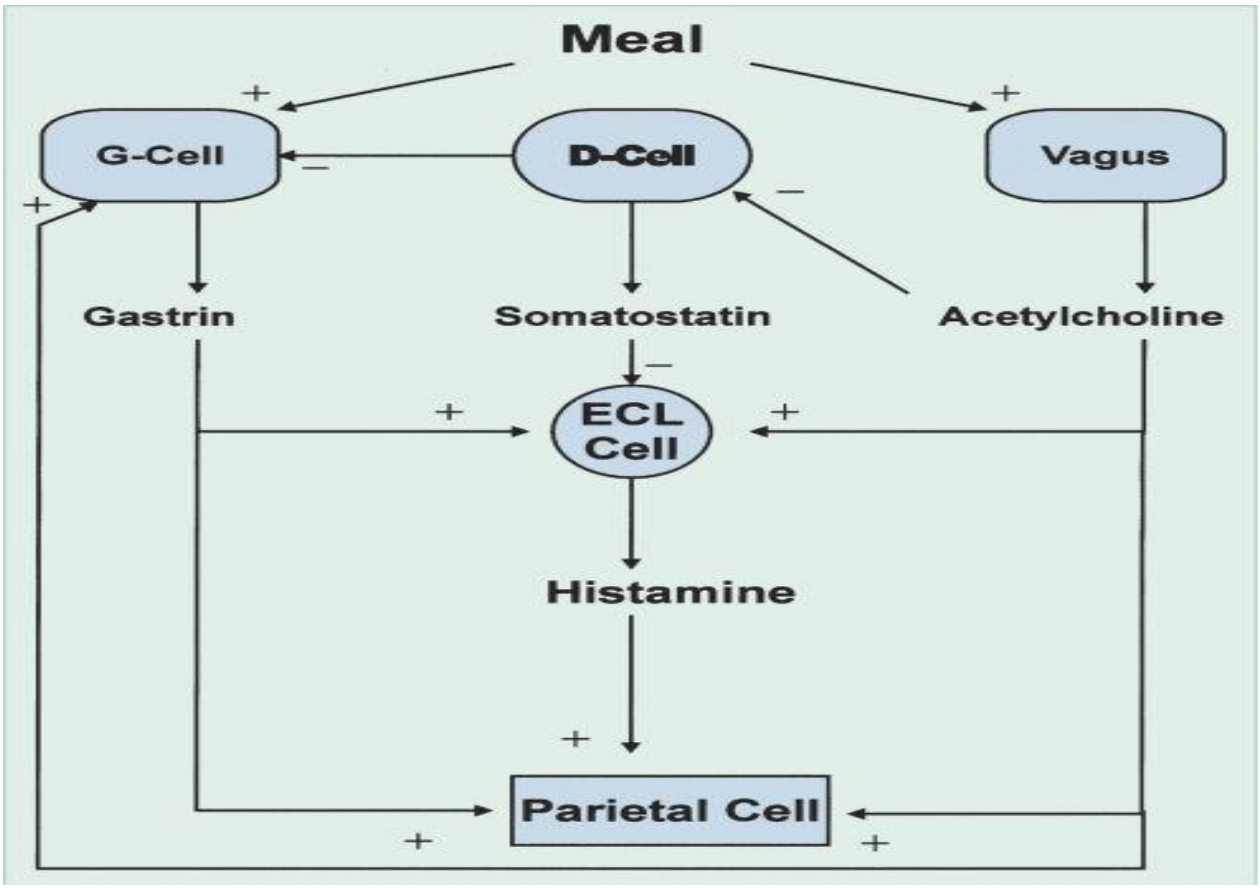
Acid secretion is mediated by three phases:

1. Cephalic phase mediated by the vagus.

2. Gastric phase mediated by the gastric distension and luminal peptides.

3. Intestinal phase which is an inhibitory phase.

The gastric acid secretion is maintained in a low basal rate during the times of fasting by D cells secreting the somatostatin which inhibits the acid secretion.



Gastric peptides:

Gastrin:

G cells located in the gastric antrum produces gastrin on stimulation. It is secreted as a prepropeptide and undergoes post-translational modification to produce biologically active gastrin peptide. The biologically active component of gastrin is the pentapeptide sequence identical to that found on Cholecystokinin. A major stimulant for the release of gastrin is protein, as well as the digestion products of protein. Its release is inhibited by the presence of luminal acid. Somatostatin has inhibitory actions on antral G cells and acts as a local inhibitor of gastrin release. Somatostatin has a tonic inhibitory effect on

gastrin release and probably mediates the negative feedback effects of luminal acid on release of gastrin.

Gastrin is the most prominent hormonal regulator of acid secretion of the gastric phase. As its acid secretory effects, gastrin has trophic effects on gastric Enterochromaffin like cells and parietal cells. Gastrin has a role in the gastric mucosal defense system.

Hypergastrinemia:

The hypergastrinemia occurs due to loss of luminal acid by loss of secretion of acid due to intake of antisecretory agents, surgical procedures such as vagotomy, gastric atrophy, perinicious anemia/uremia resulting a loss of feedback inhibition of gastrin release by luminal acid. Lack of acid causes a reduction in somatostatin release, which in turn causes increased release of gastrin from antral G cells. Gastrin levels increase inappropriately in due to hypersecretion in cases with gastrinoma. These tumors are typically located in the pancreatic head, wall of the duodenum, regional lymph nodes and secrete gastrin autonomously.

Somatostatin:

Somatostatin is produced by D cells. Somatostatin is secreted by neuroendocrine cells situated in the fundus and antrum of the stomach. Their cytoplasmic extensions are in direct contact with parietal cells and G cells,

thereby exerts its actions in a paracrine manner on gastrin release and thereby the acid secretion. Somatostatin directly inhibits acid secretion by parietal cells. It also does it by inhibiting gastrin release and also down-regulates histamine release from enterochromaffin-like cells, which indirectly inhibits acid secretion. Antral acidification is the principal stimulus for somatostatin release, whereas acetylcholine released from vagal nerve fibers inhibits its release.

Effects of H. pylori on Somatostatin:

H.pylori causes decrease in the antral D cells, causing a reduction in the somatostatin level thereby resulting in the excessive secretion of gastrin from antral G cells and resultant hypersecretion of acid. On eradication of H.pylori the antral D cell population inceases and the somatostatin level normalizes.

Gastrin-Releasing Peptide:

Bombesin was isolated from an extract obtained from skin of the amphibian *Bombina bombina.* Its mammalian counterpart is gastrin-releasing peptide (GRP). GRP is prominent in nerve endings in the acid and the gastrin secreting portions of the stomach, and in the circular muscular layer. GRP stimulates the receptors in the antral D & C cells thereby resulting in the release of somatostatin and gastrin respectively. GRP has a half life of 1.4 mins and it's rapidly neutralized in circulation by neutral endopeptidase. Bombesin possesses potent gastroprotective action mediated through an increase in gastric mucosal

blood flow. This effect is most pronounced during times of stress and injury and acts to provide additional nutrients and remove toxins from the mucosa.

Histamine:

Histamine is the common final product in parietal cell activation. Histamine is secreted and stored in the acidic granules of ECL cells and mast cells. ECL cells possess receptors for gastrin, acetylcholine, and epinephrine, all of which stimulate histamine release. The ECL cell also has receptors for somatostatin, which inhibits gastrin-stimulated histamine release. The ECL cell has a central role in activation of parietal cell and has both stimulatory and feedback pathways that maintain the release of histamine and acid secretion in a balance.

Ghrelin:

Ghrelin is a acylated peptide secreted by oxyntic cells in the fundus of the stomach. Ghrelin is the first gut peptide found to have orexigenic properties and appears to play a major role in energy homeostasis. Ghrelin appears to increase food intake through stimulation of ghrelin receptors located in the hypothalamic areas of the brain, such as the paraventricular nucleus and lateral hypothalamic area, where neuropeptide Y expressing neurons and agouti-related protein expressing neurons are localized. This ghrelin-induced activation of NPY acts as a powerful orexigenic signal that results in increased food intake,

decreased energy expenditure, and stimulation of peripheral glucocorticoid and insulin secretion, which favors the deposition of fat into adipose tissue.

Leptin:

Leptin is intimately involved in the regulation of metabolism and body weight. Source of leptin is the chief cells of the stomach in the gastrointestinal tract next to adipocytes of white fat. Leptin exerts its influence on energy and appetite via stimulation of hypothalamic neurons expressing Agouti related protein and Neuropeptide Y. Interactions among the pathways controlling both ghrelin and leptin probably play a major role in regulation of body weight.

Leptin is a powerful gastroprotective agent against damage caused by luminal irritants and has effects on insulin sensitivity, inflammation and immune function, bone formation, and angiogenesis. These additional actions of leptin outside its effects on energy balance are probably due to local rather than systemic effects and appear to be mediated via JAK-STAT phosphorylation protein kinases.

Gastric juice:

Gastric juice is a combination of secretions produced by parietal cells, chief cells, and mucous cells, swallowed saliva and refluxate from duodenum. According to the rate of gastric secretion the electrolyte composition of parietal and nonparietal gastric secretions varies. The secretion from the parietal cells is

isotonic with plasma and contains electrolytes. The solution's pH is 0.8. But the lowest intraluminal pH recorded in the stomach is 2 because of secretions that contains sodium, potassium, and bicarbonate.

Gastric Electrolyte Composition in the Human Whole Stomach

Parietal						
[H]	**[Na]**	**[K]**	**[All Cations]**	**[HCO_3]**	**[Cl]**	**[All Anions]**
148.9	—	16.9	165.8	—	166.3	166.3
Nonparietal						
[H]	**[Na]**	**[K]**	**[All Cations]**	**[HCO_3]**	**[Cl]**	**[All Anions]**
—	136.7	6.4	143.1	25.0	117.8	142.8

Intrinsic factor[IF]:

Intrinsic factor is a mucoprotein secreted by the parietal cell along with the gastric secretions that is necessary for vitamin B_{12} absorbtion in the terminal ileum. The gastric mucosa is the critical site of production for intrinsic factor, and thus patients undergoing gastrectomy or proximal stomach resection may require a monthly injection of vitamin B_{12}. Intrinsic factor deficiency develops in the setting of pernicious anemia, and these patients require vitamin B_{12} supplementation of vitamin B_{12}.

Pepsinogen:

Pepsinogens are secreted by the glands located in the gastroduodenal mucosa. They are proteolytic proenzymes and there are 2 types. The chief cells and mucous neck cells of the gastric mucosa secretes type 1 pepsinogen. Type 2 pepsinogens are secreted by surface epithelial cells in the gastric antrum and proximal duodenum. In acidic pH, both types of pepsinogen are converted to pepsin. Pepsin become inactivated at a pH of more than 5.

Mucus and Bicarbonate:

Mucus and bicarbonate are the 2 main components to neutralize gastric acid at the gastric mucosal surface. Both are produced by surface mucous cells and by mucous neck cells situated in the acid-secreting portion of the stomach and the antrum.

Mucus is a viscoelastic gel composed of 85% of water and 15% of glycoproteins. It provides a mechanical barrier, by providing the unstirred layer of water at the luminal surface of the gastric mucosa there by preventing it from injury. It is impermeable to pepsins. It is constantly renewed because it is produced continuously by mucosal cells on the one hand and solubilized by luminal pepsin on the other. Both prostaglandins derived from the constitutive cyclooxygenase-1 enzyme and nitric oxide from the eNOS and nNOS systems are critical to maintenance of the protective mucous layer and may act as

important molecular mediators of the protective mucous layer. Mucus production is stimulated by vagal stimulation, cholinergic agonists,prostglandins whereas anticholinergic drugs and nonsteroidal antiinflammatory agents inhibit its secretion. *H.pylori* secretes proteases and lipases to break down the mucin, thereby impairing the protective function of the mucous layer.

Bicarbonate secretion in gastric mucosa occurs both as active and passive process. Active form takes place in the acid-secreting portion of the stomach. In the gastric antrum, both active and passive secretion of bicarbonate occurs. The alkaline pH gradient found at the surface epithelium is the result of the unstirred layer of water contained within the mucous gel and also by the continuous secretion of bicarbonate. Gastric cell surface pH remains more than 5 until the luminal pH is less than that of 1.4.

GASTRIC ADENOCARCINOMA AND ITS FEATURES:

EPIDEMIOLOGY:

Carcinoma stomach was the commonest cancer globally in the late 20th century and is next to lung cancer among the cancer related mortality. Gastric carcinoma incidence varies geographically, with highest rates in Japan and Europe. Rates rising in India also.

In Gastric cancer male preponderance is seen and sex ratio is 2:1. Incidence also gradually increases with the mostly occurs in the seventh decade. Study on the people who migrated from high incidence areas to low incidence areas suggest that the environmental exposure , cultural , genetic factors also predispose to the occurrence of the gastric cancer.

There is a change in the trend of the anatomic location of the gastric cancers from the distal gastric unit to the proximal gastric unit in the past 30 years. The carcinoma of the Oesophagogastric junction is also rising, whereas in other areas has been decreasing.

Risk factors:

Ethnic origin is considered as a potential risk factor for the development of gastric cancer. Ethnic groups has been categorized into three risk categories:

1. Japanese, Koreans, Vietnamese, Native Americans, and Hawaiians are at the highest risk.

2. Latino, Chinese, and blacks are at intermediate risk.

3. Filipinos and whites are at the lowest risk. In addition, immigrants from high-isk to low-risk countries remain at high risk, but subsequent generations have a risk that is native to their new environment, so the environmental factors play a role.

Dietary factors have been found to be associated with an increased risk for gastric cancer, including diets high in salt, cured and smoked foods, nitrates, and nitrites. In contrast, diets high in fruits, vegetables, and antioxidants, as well as vitamins A and C and calcium, have been associated with a decreased risk for gastric cancer. Smoking also appears to be a risk factor, but the role of alcohol is less clear.

Infection with *H. pylori* has also been associated with an increased risk for the development of gastric cancer as much as 3.6-fold as compared with noninfected patients. This increase in risk was present for the development of both intestinal- and diffuse-type cancers.

Epstein-Barr virus and medical conditions such as pernicious anemia, chronic atrophic gastritis, intestinal metaplasia, gastric villous adenoma, and obesity are also associated with an increased risk of gastric cancer.

Patients who have undergone partial gastrectomy for benign gastric ulcer disease are at increased risk for gastric cancer in the stomach remnant. This risk for cancer also has a long latency period of about 15 years.

About 10% of the gastric cancer have an inherited component. Patients with hereditary nonpolyposis colon cancer syndrome and polyposis syndromes such as Peutz-Jeghers and familial adenomatous polyposis have an increased risk for the development of gastric cancer. Gastric cancer can also develop in patients with germline mutations in p53 and *BRCA2*. Finally, mutations in the cell adhesion protein E-cadherin lead to an increased risk for hereditary diffuse gastric cancer, and it has been recommended that prophylactic gastrectomy can be considered in affected individuals.

Pathology:

Adenocarcinomas constitute 95% of all gastric cancers, with gastric lymphoma, carcinoid, gastrointestinal stromal tumors, and squamous cell carcinomas making up the remaining 5%. Several pathologic classifications have been devised to describe gastric adenocarcinoma.

The Borrmann classification scheme categorizes gastric cancer into five types by its macroscopic appearance.

Type I consists of polypoid or fungating cancers.

Type II includes tumors that are fungating and ulcerated and surrounded by elevated borders.

Type III includes ulcerated lesions infiltrating the gastric wall.

Type IV cancers infiltrate diffusely.

Type V consists of those that are unable to be classified.

The Lauren classification is the most commonly used classification scheme and divides gastric cancers into two distinct types—intestinal and diffuse.

The intestinal variant arises from the gastric mucosa and is glandular in origin. Intestinal-type tumors often arise from precancerous lesions similar to other cancers of the GI tract. They are more common in men, in older patients, and in the distal part of the stomach. The intestinal variant is associated with *Helicobacter pylori* infection, chronic atrophic gastritis, intestinal metaplasia, and dietary factors.

In contrast, the diffuse-type pathology appears to arise from the lamina propria, is associated with an invasive growth pattern, and is less related to environmental factors. Diffuse-type tumors are more common in younger patients and in the proximal part of the stomach. These tumors are characterized by noncohesive malignant cells diffusely infiltrating the stomach with minimal

to no gland formation. They tend to spread rapidly in the submucosa, as well as by transmural extension and lymphatic invasion. Peritoneal metastases are also more common with diffuse-type gastric cancers. These cancers have increased in incidence and are associated with a worse prognosis than the intestinal variants.

The World Health Organization has further characterized gastric adenocarcinoma into five categories, depending on the degree of intestinal metaplasia. The classification includes adenocarcinoma (intestinal and diffuse), signet cell, mucinous, tubular, and papillary.

Traditionally, most gastric cancers were found in the antrum; however, in the 1980s and 1990s, antral cancers declined and the proportion of proximal tumors and those of the cardia have increased. In general, cancer of the lesser curve is more common than cancer of the greater curve. In almost 10% of cancers, the tumor can involve the entire stomach with malignant cells infiltrating beyond the apparent mass, a condition termed *linitis plastica.* This entity portends an especially poor prognosis, with 5-year survival being very unusual.

Early gastric cancer is an entity characterized by tumor confined to the gastric mucosa or submucosa. Advanced gastric cancers are the ones extending

beyond the submucosal level. Extensive screening programs are required to detect the early gastric cancer.

Clinical features:

Early gastric cancer mostly asymptomatic, sometimes produces nonspecific symptoms. Consequently, nearly 80% to 90% of patients are initially seen with locally advanced or metastatic disease. When early evaluation does take place, most patients complain of weight loss, anorexia, and abdominal pain.

Anemia secondary to chronic blood loss is also common, but overt upper gastrointestinal bleeding is uncommon unless the tumors are large and ulcerated. Dysphagia occurs predominantly in patients with proximal cancers, whereas nausea, vomiting, and symptoms of gastric outlet obstruction are more common with distal tumors that obstruct the lumen. Early satiety is especially prominent in patients with *linitis plastica* because of the nondistensibility of the stomach.

Patients with early gastric cancer seldom have significant physical findings. Patients with more advanced disease may have a palpable abdominal mass, as well as ascites and cachexia. Patients with metastatic disease may exhibit Blumer's shelf nodules on rectal examination or Krukenberg tumors on pelvic examination, periumbilical lymphadenopathy called as Sister Mary

Joseph's node or peritoneal metastases, and palpable supraclavicular adenopathy called as Virchow's node.

Diagnosis:

Patients with newly diagnosed gastric cancer should undergo

1. A complete history and physical examination.

2. Laboratory studies, including a complete blood count, platelets, liver function tests, coagulation profile[prothrombin time, activated partial thromboplastin time] renal function tests

Prothrombin time:

The prothrombin time measures the integrity of the extrinsic coagulation pathway which is iniated by the tissue factor and finally leading to the formation of fibrin clot.

Method:

The citrated, platelet-poor plasma has been used for this. The qulity of the blood specimen the most important factor determining the result.The specimen obtained from the patient should be analysed within 24hrs for prothrombin time. The plasma is incubated at 37°C along with the reagent containing the

thromboplastin. Then calcium chloride is added to that mixture following that the time required for the formation of clot is measured in seconds / as a ratio with the normal. The INR is the international normalized ratio developed by WHO for easy comparison of the prothrombin time, by measuring the prothrombin time against the international reference preparation of thromboplastin produced by WHO from human brain extract. Whereas the prothrombin time measured using other varieties of tissue factor are standardized by the following formula:

$INR=\{Patient\ PT/Mean\ normal\ PT\}^{ISI}=[Prothrombin\ time]^{ISI}$.

3. Chest radiography.

4. Computed tomography of the abdomen.

5. Computed tomography of the chest in case of proximal tumors involving the proximal gastric unit.

6. Computed tomography/ultrasonography of the pelvis in females.

7. Upper endoscopy and biopsy with the goal of a tissue diagnosis and anatomic localization of the tumor.

8. Serum tumor markers, including carcinoembryonic antigen (CEA), CA 19-9, CA-125, CA 72-4, and β-human chorionic gonadotropin (β-HCG), can be elevated in patients with gastric cancer, although the individual sensitivities are

generally low—in the 40% to 50% range. The sensitivity of these tumor markers is significantly improved, however, when several are elevated. Furthermore, in patients with known gastric cancer, markedly elevated tumor markers may also signify aggressive disease or tumor burden.

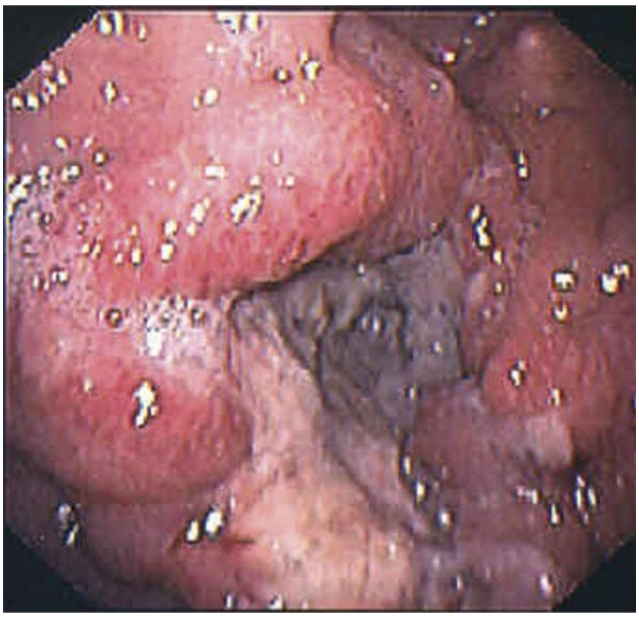
This work-up will usually allow one to classify patients into one of two groups—those with locoregional disease (stage I to III or M0) and those with systemic metastases (stage IV or M1).

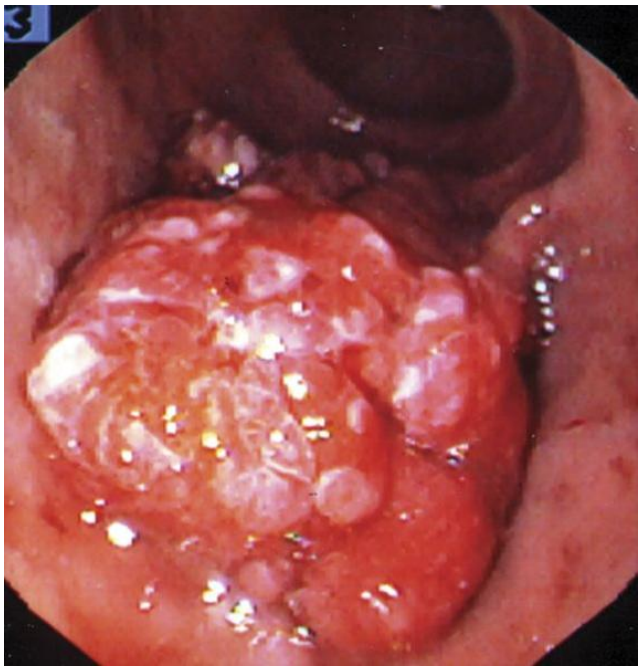
Patients with locoregional disease are further stratified according to resectability, functional status, and comorbid conditions, with further evaluation often including laparoscopy and endoscopic ultrasound (EUS). Patients with metastatic disease are considered for palliative therapy, depending on their symptoms and functional status.

Upper GI endoscopy (EGD) with biopsy remains the modality of choice for the diagnosis of gastric cancer. Tumor location and the size and extent of mucosal involvement are readily ascertained, provided that the gastric lumen is not obstructed by the tumor. In more than 95% of patients, four to six tissue biopsy specimens and brushings are sufficient to establish the diagnosis, although this can often be difficult in patients with linitis plastica. In advanced disease, EGD can be a means to provide palliative therapy, including laser ablation, dilatation, and stenting, although the precise role of these modalities is still evolving.

EUS has also become a valuable staging tool for patients with locoregional disease. In experienced hands, EUS can often accurately determine the depth of invasion and nodal status in patients with gastric cancer. The overall accuracy of EUS in staging is about 75% to 80%, but it is significantly operator and institution dependent. Staging of T1 (80%) and T3 (90%) lesions is quite accurate, but EUS is limited in accurately staging T2 lesions (35% to 40%). Nodal staging is also less accurate with EUS, but newer techniques have increased its accuracy 50% to 85%. EUS-guided fine-needle aspiration for additional tissue diagnosis has also been performed, but experience with this technique is limited and usually confined to large referral centers.

Various appearances of adenocarcinoma stomach in endoscopy are:





Computed tomography of the abdomen and pelvis is also very useful and commonly used in the preoperative work-up of patients with gastric cancer. Contrast-enhanced CT can detect metastases to the liver and peritoneum, local invasion into adjacent structures, and regional and distal lymphadenopathy, as well as ascites suggesting peritoneal disease. The overall accuracy in assessing tumor stage is 66% to 77%, but its accuracy in correctly staging nodal disease is much more variable, from 25% to 86%. CT is also limited in detecting early gastric tumors or small (<5 mm) peritoneal or hepatic metastases.

Magnetic resonance imaging has also been shown to be as accurate as Computed Tomography in the staging and detection of gastric cancer. Though expensive and associated with motion artifact, several studies have reported MRI as being slightly superior to CT in the T staging of tumors, with

overall T staging accuracy between 73% and 88%. Although MRI may also be superior to CT in N staging (73% versus 65%), both techniques suffer from under-staging. MRI has also been shown to be superior to CT in the detection of liver, bone, and peritoneal metastases. Nevertheless, the continued improvement in CT scanning equipment and technique, combined with the expense and relative less availability of routine MRI, continues to result in CT being the preferred staging modality for gastric cancer at most institutions.

Positron emission tomography with [F]fluorodeoxyglucose is increasingly being used in the preoperative staging of GI cancers. Though fairly well established in the work-up of colorectal cancer and more recently esophageal cancer, experience with PET scanning in patients with gastric cancer is limited. Preliminary data suggest that PET may be very useful in identifying the primary gastric cancer (90% to 95% sensitivity) and perhaps in monitoring treatment response. Its usefulness in determining N stage is more variable, however (35% to 60% sensitivity), and in general, PET is more accurate in detecting N2- and N3-level nodes because they are further away from the primary tumor. Nevertheless, additional studies are needed before PET scanning can be recommended as a *routine* diagnostic and staging tool for gastric cancer.

Diagnostic laparoscopy remains a popular diagnostic modality for the staging of gastric cancer and is especially helpful in detecting small-volume peritoneal and liver metastases. It has been demonstrated in several studies that

the sensitivity of laparoscopy in detecting liver metastases is as high as 85% to 96%, though somewhat lower in detecting peritoneal disease. In general, between 23% and 37% of patients with gastric cancer are up-staged by the use of staging laparoscopy and therefore potentially spared a laparotomy.

Laparoscopic ultrasound (LUS) has also been used in hope of further improving the capability of laparoscopic exploration. The specific benefit of LUS over high-quality CT scanning and laparoscopy is unclear, however, and the use of LUS in the gastric cancer staging remains limited.

Cytologic analysis of washings obtained from peritoneal cavity may identify patients with occult carcinomatosis, and many institutions have adopted cytologic analysis of peritoneal washings obtained at laparoscopic staging or even during laparotomy as part of the diagnostic algorithm. Prognosis of the patients with positive findings on peritoneal cytology are similar to those with occult visceral metastatic disease. Cytologic analysis may result in false-positive results, however, and because some reports fail to confirm the prognostic significance of positive cytologic findings, it has not been universally adapted.

Staging of gastric cancer:

The most widely used staging system is the American Joint Commission for Cancer TNM system, which involves standard evaluation of the tumor (T),

regional lymph nodes (N), and the presence of metastatic disease (M). The T stage is divided into four levels, depending on the depth of invasion, with recent subdivision of the T2 level into T2a (invasion of the muscularis propria) and T2b (invasion of the subserosa). The N status reflects the number of lymph nodes involved, with the requirement that at least 15 lymph nodes be removed for the patient to be properly staged. Of note, N3 cancers (>15 metastatic lymph nodes) are considered stage IV. The Japanese staging system defines nodal stage by anatomic location and proximity to the tumor. This system is based on 16 nodal stations and is complicated and difficult to use, particularly in institutions where gastrectomies are rarely performed.

The AJCC classification system of the adenocarcinoma of the stomach as follows:

PRIMARY TUMOR [T]

TX	PRIMARY TUMOR CANNOT BE ASSESSED
T0	NO EVIDENCE OF PRIMARY TUMOR
Tis	CARCINOMA IN SITU;INTRAEPITHELIAL TUMOR WITHOUT THE INVASION OF THE LAMINA PROPRIA
T1	TUMOR INVADES LAMINA PROPRIA, MUSCULARIS MUCOSAE, OR SUBMUCOSA
T1a	TUMOR INVADES LAMINA PROPRIA OR MUSCULARIS

	MUCOSAE
T1b	TUMOR INVADES SUBMUCOSA
T2	TUMOR INVADES MUSCULARIS PROPRIA
T3	TUMOR PENETRATES SUBSEROSAL CONNECTIVE TISSUE WITHOUT THE INVASION OF THE VISCERAL PERITONEUM/ADJACENT STRUCTURES
T4	TUMOR INVADES THE SEROSA AND ADJACENT STRUCTURES
T4a	TUMOR INVADES THE SEROSA
T4b	TUMOR INVADES THE ADJACENT STRUCTURES

REGIONAL LYMPH NODES:

NX	REGIONAL LYMPH NODES CANNOT BE ASSESSED
N0	NO REGIONAL LYMPH NODE METASTASIS
N1	METASTASIS IN 1-2 REGIONAL LYMPHNODES
N2	METASTASIS IN 3-6 REGIONAL LYMPHNODES
N3	METASTASIS IN 7/MORE REGIONAL LYMPHNODES
N3a	METASTASIS IN 7-15 REGIONAL LYMPHNODES
N3b	METASTASIS IN 16 OR MORE REGIONAL LYMPHNODES

DISTANT METASTASIS:

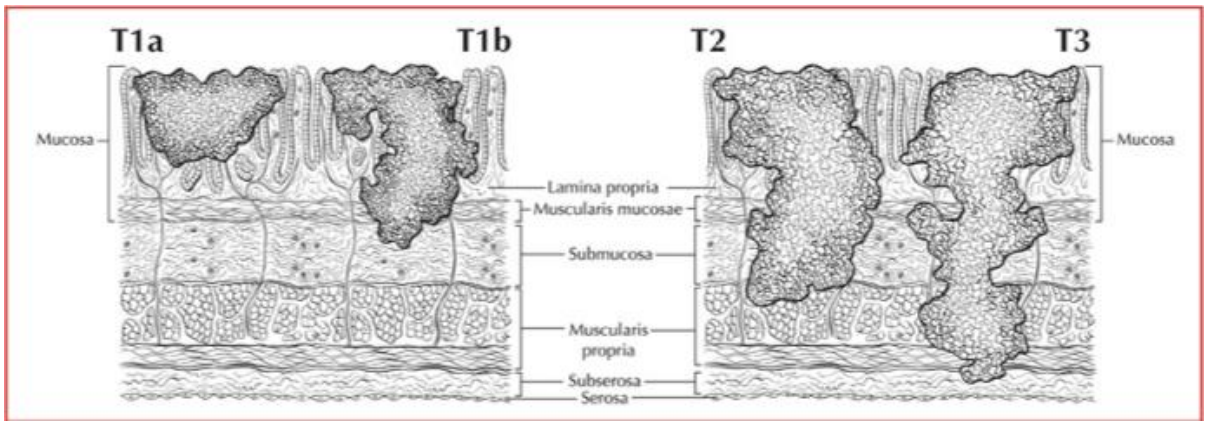
M0	NO DISTANT METASTASIS
M1	DISTANT METASTASIS

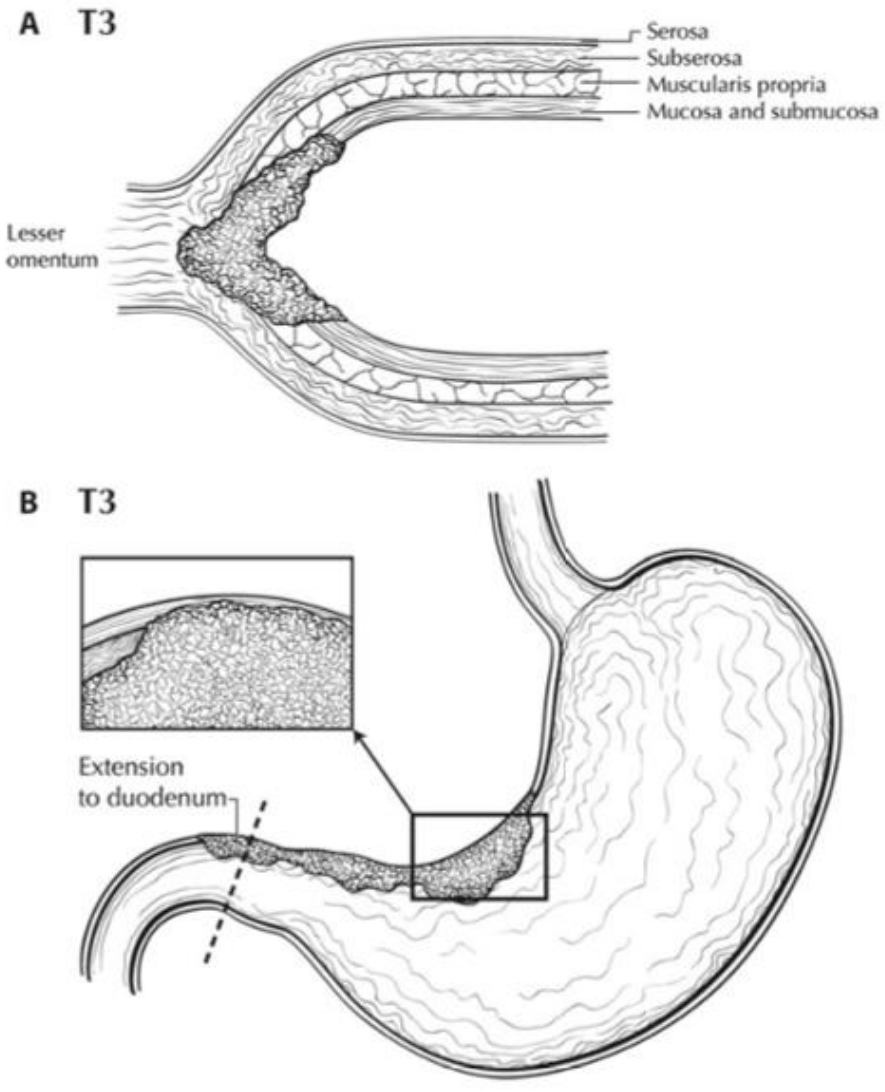
ANATOMIC STAGE:

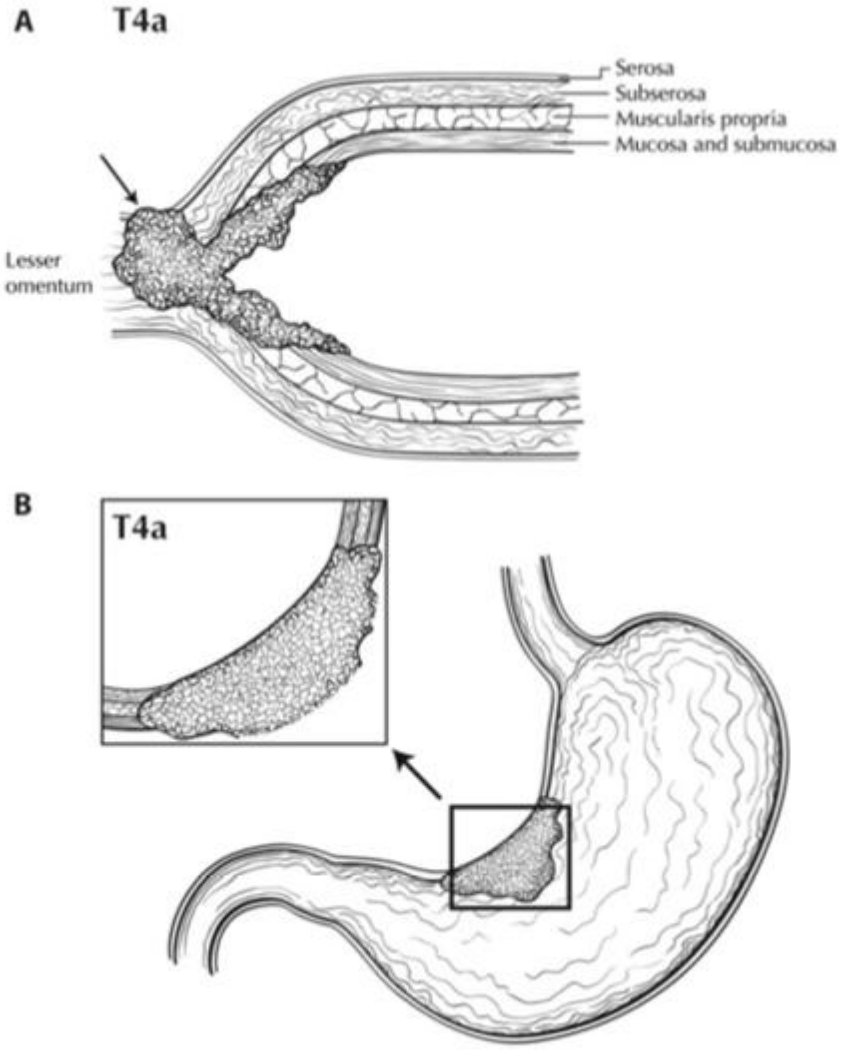
STAGE 0	Tis	N0	M0
STAGE IA	T1	N0	M0
STAGE IB	T2 T1	N0 N1	M0
STAGE IIA	T3 T2 T1	N0 N1 N2	M0
STAGE IIB	T4a T3 T2	N0 N1 N2	M0

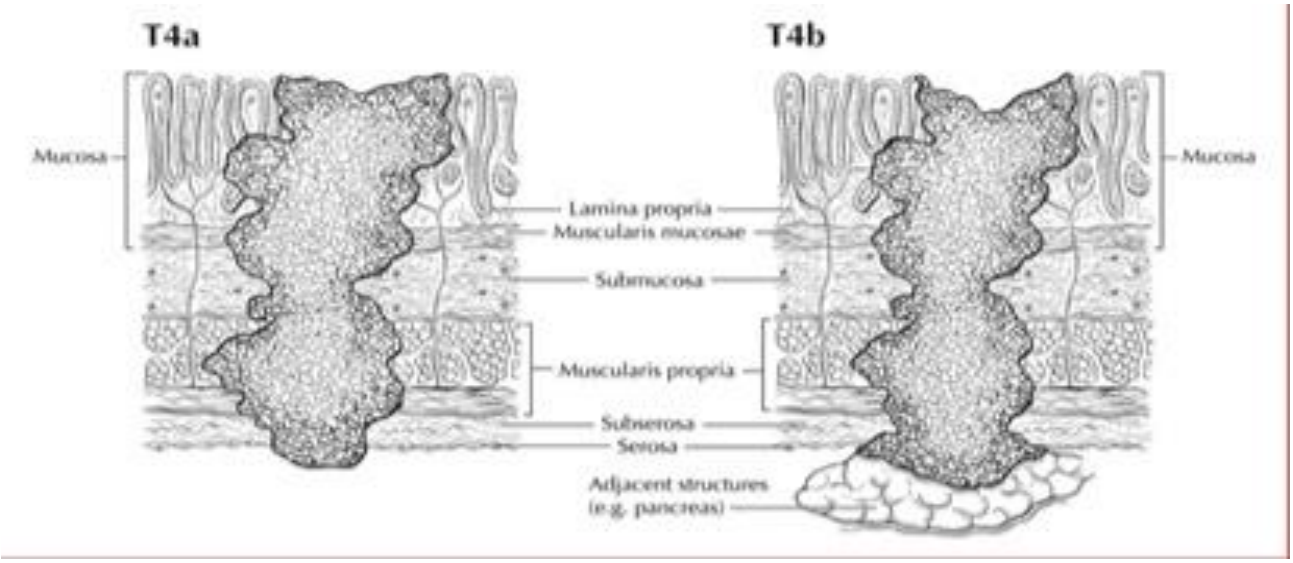
	T1	N3	
STAGE IIIA	T4a T3 T2	N1 N2 N3	M0
STAGE IIIB	T4b T4b T4a T3	N0 N1 N2 N3	M0
STAGE IIIC	T4b T4a	N2&3 N3	M0
STAGE IV	Any T	Any N	M1

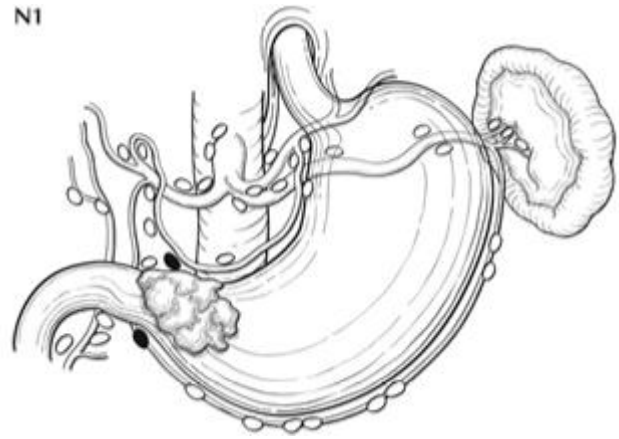
FOLLOWING PICTURES SHOWS T STAGING OF GASTRIC CANCER:

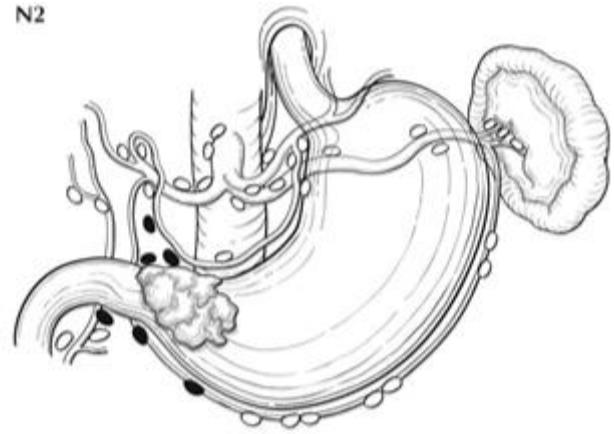


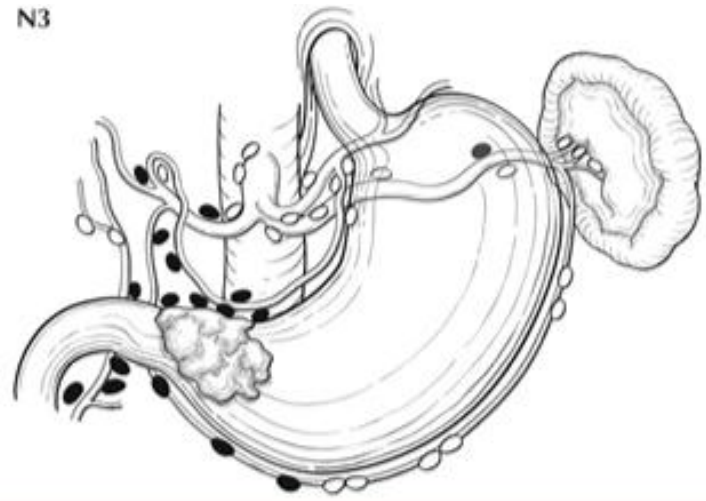



A
T4a
Serosa
Subserosa
Muscularis propria
Mucosa and submucosa
Lesser
omentum
B
T4a


T4a
T4b
Mucosa
Mucosa
Lamina propria
Muscularis mucosae
Submucosa
Muscularis propria
Subserosa
Serosa
Adjacent structures
(e.g. pancreas)

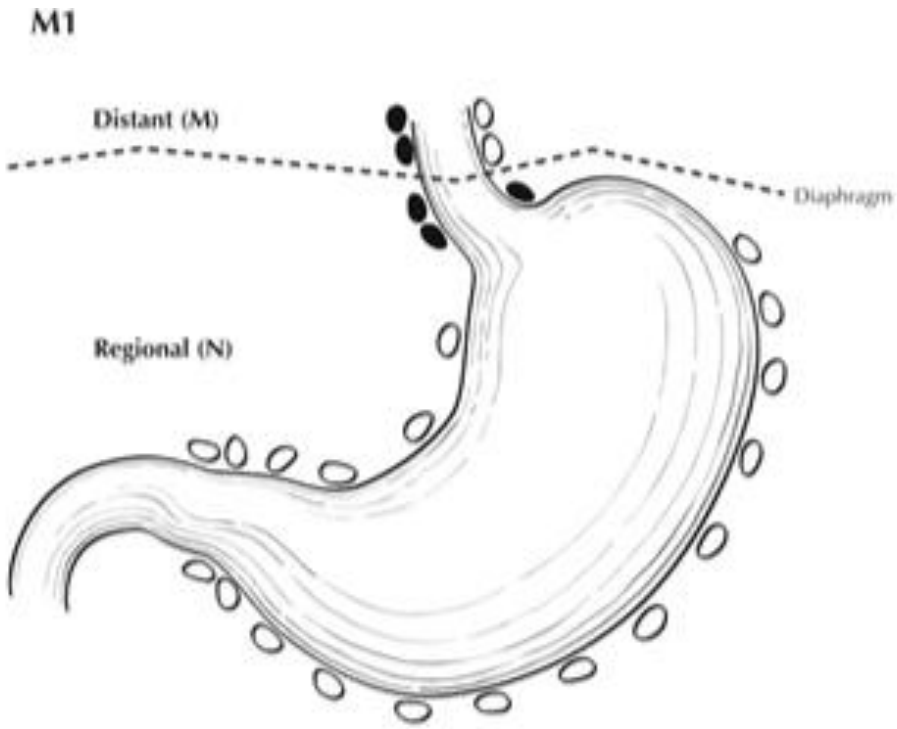






THE ABOVE PICTURES SHOWS THE N STAGING OFGASTRIC CANCER.

THE PICTURE DEPICTS THE DISTANT METASTASIS IN GASTRIC CANCER.



SURGICAL TREATMENT:

Complete operative resection remains the only potentially curative modality for gastric adenocarcinoma. The results of resection for early gastric cancer are excellent; however, the majority of patients present with symptomatic advanced lesions. Operative decisions, then, focus on the most effective procedure that offers potential for cure or on how to achieve the maximal palliation with the minimal morbidity.

Many patients who have advanced gastric adenocarcinoma may not be medically fit for any procedure. More difficult, however, is the patient who can

tolerate a procedure and has minimal symptoms, but by preoperative studies (e.g., computed tomography [CT] or laparoscopy) has incurable disease (e.g., ascites, peritoneal extension, or liver metastases). Such patients should be strongly considered for nonoperative treatment.

Extent of Gastric Resection:

The extent of gastric resection for adenocarcinoma of the stomach is mainly predetermined by the site and extent of the primary neoplasm. For those patients in whom adequate (4 to 6 cm) margins beyond the lesion can be obtained, a more limited gastric resection provides the same survival result for the patient and diminishes perioperative morbidity. The extent of the margin is rarely the limiting factor in survival. Patients rarely die of local marginal recurrence only, and similarly, patients who are likely to have positive resection margins are usually those who have large penetrating (T3) or node-positive lesions. The need for a total gastrectomy, however, to encompass all the disease within the stomach should never be a factor in precluding proceeding with the operation.

Extent of Lymph Node Dissection

The involvement of lymph nodes is predicated on the site of the primary lesion within the stomach. Lesions can then be much better defined as to the extent of the dissection. This is true even in lesions that involve the majority of

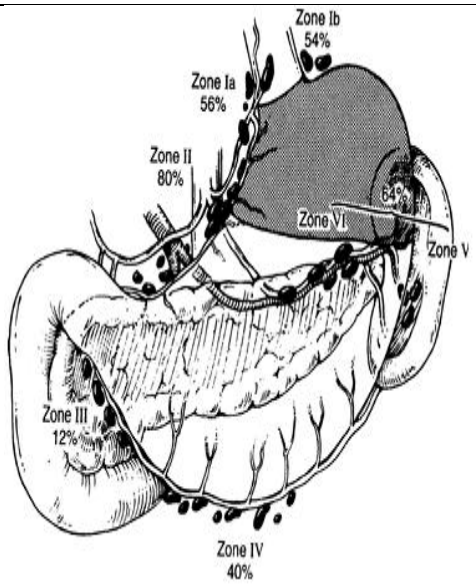
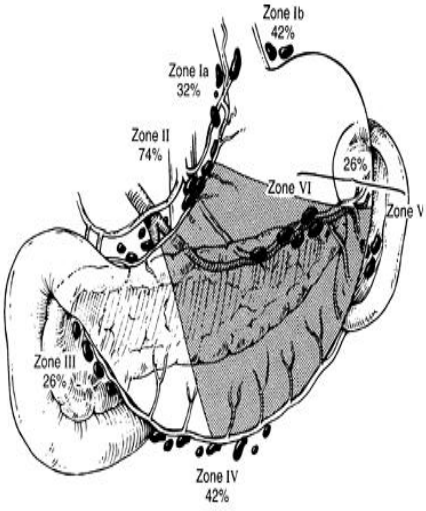
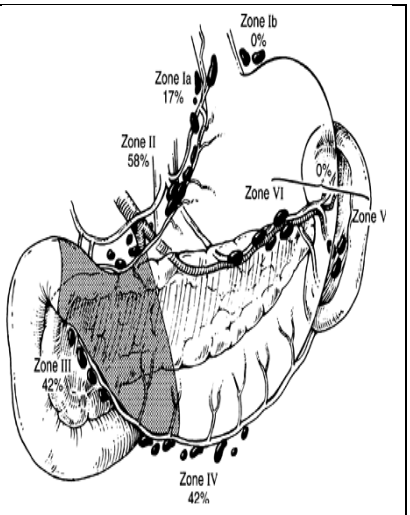
the stomach. Where the more extensive lesion is identified is the area in which the greater nodal dissection is required.

The improved survival results seen by the Japanese authors have been suggested to be due to the more extended nodal dissection. It is important to emphasize the change in the staging system with a requirement of atleast 15 nodes to be identified for staging.

Staging of nodal metastasis is characterized according to the number of positive nodes (PNs), with PN1 reflecting one to six positive nodes; PN2, seven to 15 positive nodes; and PN3, more than 15 positive nodes.

Use of Extended Organ Resection:

It appears clear that any extended resection, whether of the spleen, pancreas,colon, or a major artery, is accompanied by increased morbidity and mortality with no survival benefit. Adjacent organ resection of the spleen, pancreas, or tranverse mesocolon, should be reserved for lesions, especially N0, in which it is required for complete local resection of the primary tumor.

		
Proximal lesion with nodal metastasis	Mid gastric lesion with nodal metastasis	Distal lesion with nodal metastasis

Operative Preparation:

Total gastrectomy remains a major operation in the hands of all but the experienced gastric surgeon. It is practice to perform a total gastric resection when 4 to 6 cm of negative margins cannot be obtained from the primary tumor. An extended dissection (D2) is the nodal dissection of choice. A minimum of 15 nodes should be identified and sampled for accurate staging.

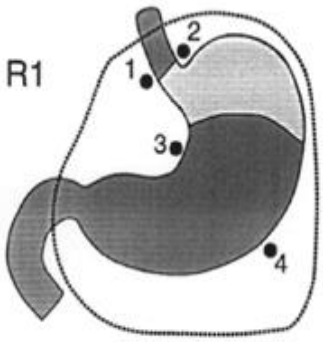
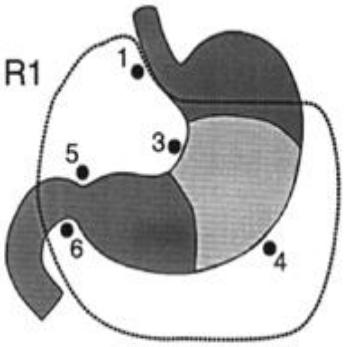
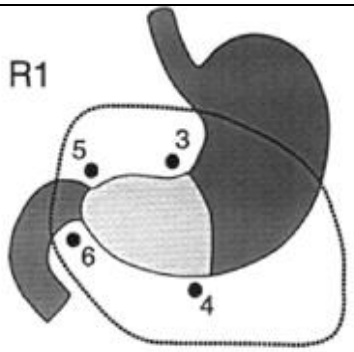
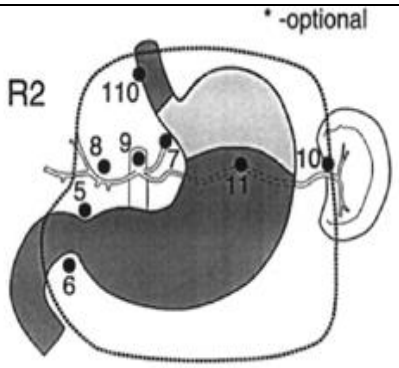
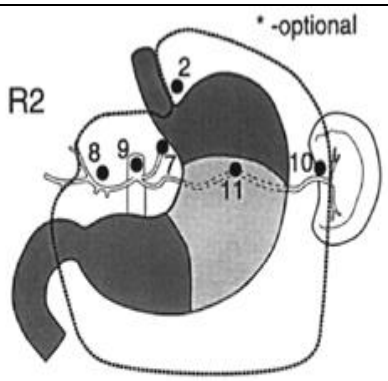
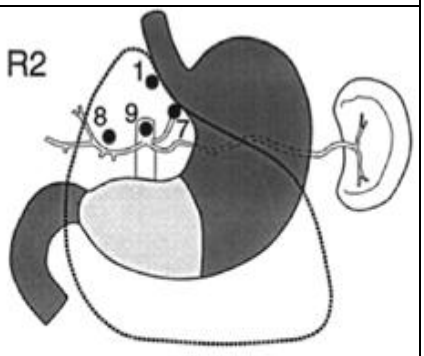
With preoperative staging of this nature, consideration as to curative versus noncurative operation can be embarked on. On occasion, especially for distal lesions, palliative operations to relieve obstruction or bleeding are justifiable; however, significant bleeding is relatively rare in conventional gastric adenocarcinoma.

Patients who have undergone endoscopic ultrasound and laparoscopy and have been shown to have advanced T3 lesions apparently confined to the stomach can be considered for investigational regimens of preoperative chemotherapy.

Preoperative Planning:

The patient is evaluated for tolerance for a potential major upper abdominal operation. If the gastroesophageal junction is involved and there is a likelihood that a thoracic approach will be required,

preoperative pulmonary function may be necessary. Preoperative antibiotics, usually with a cephalosporin, are used at the time of induction, generally for a single dose, dependent on the half-life of the drug used and the length of the operation, with the intent of diminishing wound infection.

Lymphatic resection for the gastric cancer according to its location		
Proximal stomach	Middle of the stomach	Distal stomach
 1 Rt cardiac 3 Lesser curvature 2 Lt cardiac 4 Greater curvature (& short gastric)	 1 Rt paracardial 5 Suprapyloric 3 Lesser curvature 6 Infrapyloric 4 Greater curvature	 3 Lesser curvature 5 Suprapyloric 4 Greater curvature 6 Infrapyloric
 5 Suprapyloric* 9 Celiac 6 Infrapyloric* 10 Splenic hilar 7 Lt gastric 11 Splenic 8 Hepatic 110 Paracardial (cardiac lesion)	 2 Lt paracardial* 9 Celiac 7 Lt gastric 10 Splenic hilar* 8 Hepatic 11 Splenic	 1 Rt paracardial 8 Hepatic 7 Lt gastric 9 Celiac

Positioning:

The patient is placed in supine position, with consideration given to the possibility of left or right thoracic approach in proximal gastroesophageal lesions. A sandbag can be placed beneath the left costal margin to elevate it, and the lower left chest prepared for an extension directly into the left chest. A split-lumen endotracheal tube is placed in all patients in whom thoracotomy is likely. In the majority of patients undergoing total gastrectomy, the lesion is confined to the stomach and an abdominal approach is adequate.

A long midline incision or a bilateral subcostal incision is preferable according to the operating surgeon. Both provide excellent exposure to the upper abdomen. An alternative approach, a left thoracoabdominal incision, is preferred for gastroesophageal junction lesions. Once access to the abdomen is obtained, careful examination for the extent of disease is performed. Important considerations are the presence of peritoneal metastasis or liver involvement. Remote lymph node involvement precludes progression to a radical procedure.

The first approach in the dissection is the section of the greater omentum from the colon. This is performed by using the cautery or the scissors and entering into the anterior leaf of the mesocolon. It can take a small amount of time to obtain the correct plane and to skeletonize mesocolonic vessels. On occasion, local invasion or adherence is present and mesocolonic resection is required. The standard dissection is continued back to the inferior border of the

pancreas, and the pancreatic capsule is dissected upward. Branches to the right gastroepiploic vessels are divided just at the inferior border of the pancreas. The extension is continued out laterally, along with the superior aspect of the pancreas, skeletonizing the splenic artery and dividing the short gastric vessels close to the spleen. At this point it is often easier to change the approach and begin by dissecting the lesser omentum from the undersurface of the liver, extending back to the right crus and mobilizing the right aspect of the gastroesophageal junction.

At this point division of the duodenum is simple, usually performed with two straight Kocher clamps or the GIA stapler, taking care to invaginate the closure. Closure of the duodenum with the GIA-60 stapler and close the divided stump of it with interrupted horizontal 3-0 monofilament absorbable mattress sutures.

Division of the duodenum allows elevation and rotation of upward and forward of the stomach and easy access to the dissection of the node-bearing areas.

Dissection in the porta can begin from above, isolating the hepatic artery bifurcation, bringing the node-bearing tissue inferiorly, and dissecting the portal vein, to the left of the left hepatic artery and in the area between the common hepatic and the superior border of the pancreas. This dissection can be swept back to the celiac axis, picking up the dissection of the superior border of the pancreas at the junction of the splenic artery with the celiac. The left gastric artery is then divided at its origin.

Dissection from above along the right crus allows the aortic junction of the celiac axis to be identified and cleared. The extent of the dissection of the splenic hilum depends on the extent of disease present. The short gastric vessels are identified and ligated close to the spleen, the colonic attachments to the spleen having been reflected inferiorly early in the procedure.

The left crus is identified and all tissue reflected from it. The left adrenal gland should be clearly identified and preserved from harm. At this point, with the entire stomach mobilized, the left gastric artery can be divided at its origin and the entire stomach lifted forward. The paracardial lymph nodes are reflected inferiorly. The gastroesophageal junction is mobilized, and to divide the esophagus using a soft Satinsky atraumatic vascular clamp for stabilization.

Frozen section of the proximal margin is performed if there is concern about proximal extension. In our data, it appears that a positive microscopic margin is a negative prognostic factor in patients who have one to five nodes positive. However, if the patient has more than five positive nodes, the positive margin is no longer an independent predictor of poor survival.

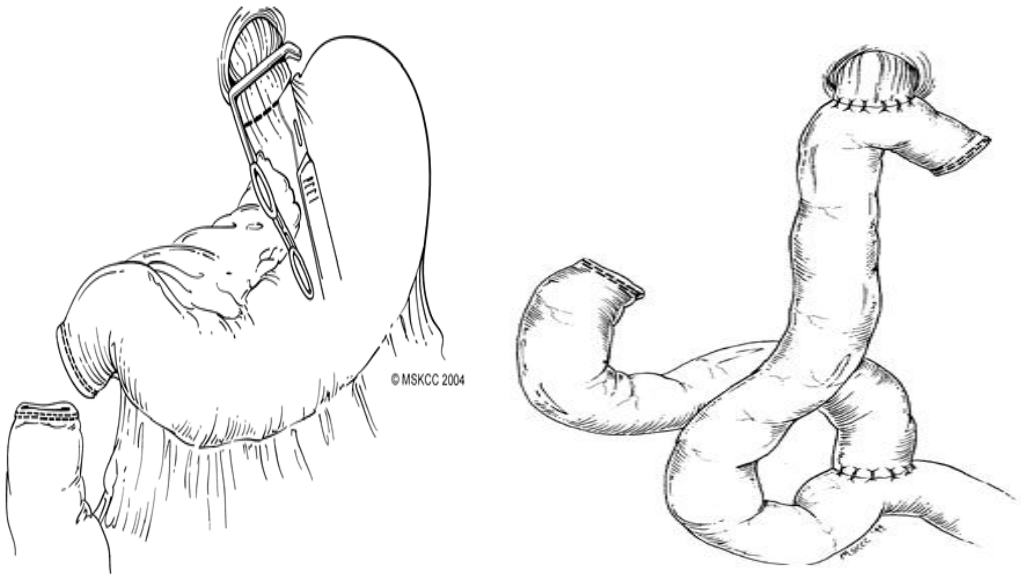
Reconstruction:

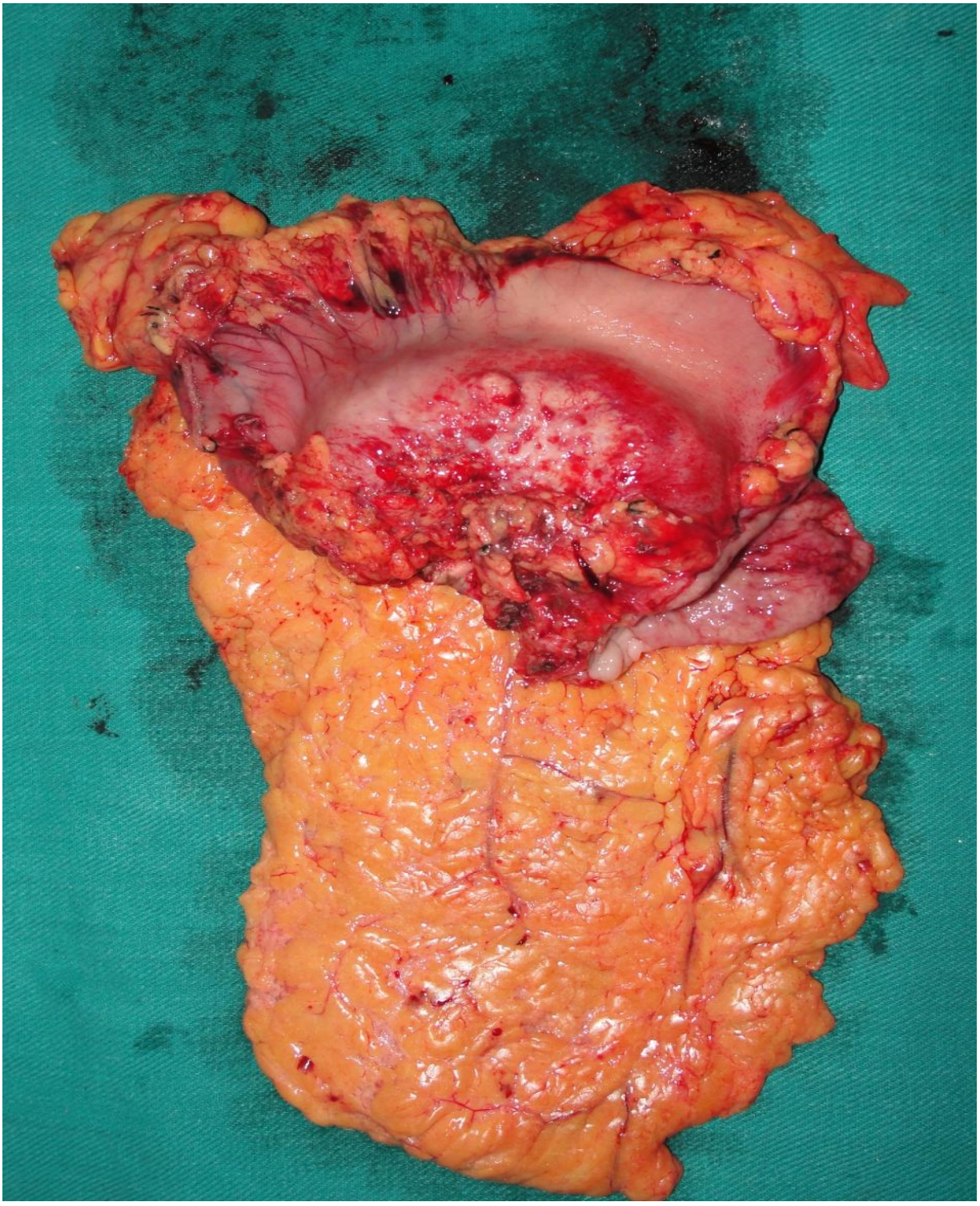
Standard reconstruction is usually by the Roux-en-Y method, using a loop of jejunum anastomosed from the end of the esophagus to the side of the jejunum. This loop should be at least 40 cm from the subsequent jejunojejunal anastomosis. The length of 40 to 50 cm should minimize esophageal reflux. In preparation of the jejunal loop, isolate a loop of jejunum with its vascular

supply and divide that with the GIA stapler. This then allows the passage through the retrocolic approach to place it in juxtaposition to the esophagus. Anastomosis of the esophagus to the jejunum.preferably a single layer of running polydioxanone sutures taken with large, full-thickness bites. Postoperative management involves standard maintenance of fluid and electrolyte balance. A nasogastric tube, which may have been passed at the time of the procedure, is removed on the first postoperative day.

Unless fever or ileus develops, the patient is allowed to take oral fluids on the third day and can be given nutrient by the fifth or sixth day. Any concern clinically for an anastomotic leak can be confirmed by a Gastrografin swallow. If a leak occurs, oral intake is limited until the patient's status is evaluated. Only a clinically significant leak is formally drained.

The picture depicts total gastrectomy andreconstruction.





Subtotal gastrectomy:

The only thing that differs subtotal gastrectomy from total gastrectomy is the gastric resection. The line connecting a point approximately 2 cm distal to the gastroesophageal junction on the lesser curvature and a point about 5 cm proximal to the tumor's upper border on the greater curvature of the stomach is selected.

Straight bowel clamps are placed on the greater curvature side of the stomach for a distance of approximately 6 to 8 cm, and the stomach is divided between these clamps with the knife. This cut surface of stomach will serve as the site of anastomosis in the fashion of Hofmeister. The remaining stomach from the tips of the straight clamps to the chosen point on the lesser curvature is divided with the GIA stapler to create a short Hofmeister shelf. The staple line is then inverted with a running monofilament suture.

The specimen is passed to a sterile back table in the operating room where it is carefully oriented for the pathologist. from the specimen and to assign their numerical stations for the pathologist. This ensures that the final pathology report includes not only the total number of positive and retrieved lymph nodes but also their location(s). Intraoperative frozen sections of the proximal gastric and distal duodenal margins are obtained prior to initiating the reconstruction.

Reconstruction:

The two most common types of reconstruction: the Billroth II loop gastrojejunostomy and the Roux-en-Y gastrojejunostomy.

A loop gastrojejunostomy may be constructed by bringing the jejunum to the gastric pouch either in front of the transverse colon called as antecolic anastomosis or through a defect in the transverse mesocolon called as retrocolic anastomosis. In either case, a proximal loop of jejunum just distal to the ligament of Treitz that reaches the stomach without tension or angulation should be chosen. It is particularly important to avoid an excessively lengthy afferent limb draining the biliary and pancreatic secretions as such a limb is prone to kinking and occlusion, with the resultant afferent loop syndrome. After gastric resection, an antecolic anastomosis drains as well as a retrocolic anastomosis, and because it is simpler to construct, we prefer the antecolic position.
The gastrojejunal anastomosis may be performed in either a stapled or a hand-sewn fashion.

The jejunal loop is brought up to the gastric pouch in a side-to-side fashion with the proximal end of the jejunum apposed to the lesser curvature side of the opening in the stomach. An outer, posterior row of interrupted, absorbable seromuscular (Lembert) sutures is placed between the posterior gastric wall and the jejunum. The straight clamp is removed from the stomach and an incision is made in the jejunum of slightly shorter length than the gastrotomy with the electrocautery.

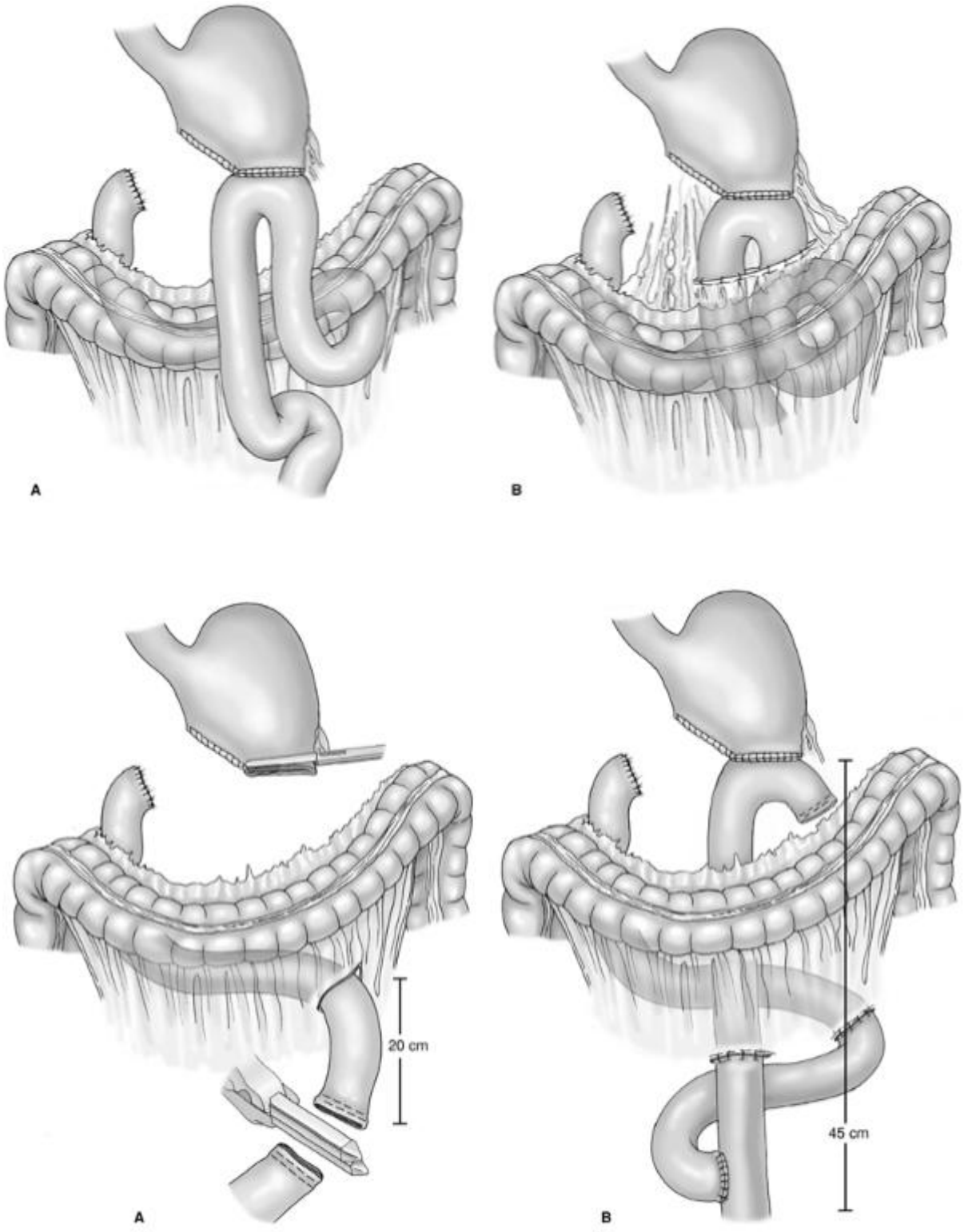
The inner, posterior layer of the anastomosis is performed with a running 3-0 PDS suture in simple over-and-over fashion, including the full thickness of both the stomach and jejunal walls. The inner layer anastomosis is continued anteriorly as a running Connell suture, which inverts the anastomosis. Of note, a nasogastric tube is advanced by the anesthesiologist and guided through the gastric remnant just into the efferent limb of the jejunum prior to completing the anterior layer of the anastomosis. The anterior portion of the gastrojejunostomy is completed with the placement of interrupted, absorbable Lembert sutures. Special care should be directed to the placement of a three-cornered Lembert suture at the junction of the lesser curvature gastric staple line and the gastrojejunostomy.

A Roux-en-Y reconstruction with a small residual gastric pouch in order to minimize the incidence of bile reflux gastritis and esophagitis in the patient. In fact, it is important to ensure that the residual gastric pouch after subtotal gastrectomy is not too large in order to minimize the risk of delayed gastric emptying. The jejunum is divided approximately 20 cm distal to the ligament of Treitz and brought up to the stomach through a defect created to the left of the middle colic vessels in the transverse mesocolon. The gastrojejunal anastomosis is performed as described for the loop anastomosis. Intestinal continuity is restored with a side-to-side jejunojejunostomy at a distance of 45 cm distal to the gastrojejunostomy in order to prevent the reflux of biliary and pancreatic secretions into the gastric remnant.

The jejunojejunostomy may be performed in a stapled or a hand-sewn fashion. For a stapled anastomosis, two small enterotomies are created in the antimesenteric borders of the small intestine. One fork of a GIA stapler is placed in each intestinal lumen and then fired. The common enterotomy is then closed with either a TA stapling device or a full-thickness running monofilament suture after inspection of the staple line for hemostasis.

Although many surgeons routinely place intra-abdominal drains and/or feeding tubes at the time of gastrectomy, we have recently taken a much more selective approach in this regard. We would consider the placement of a closed-suction intra-abdominal drain, for instance, in the patient in whom extensive peripancreatic dissection or partial pancreatectomy is necessary for a margin-negative resection. Similarly, we no longer routinely maintain feeding jejunostomy tubes in our patients after gastrectomy. Although many of our patients have feeding jejunostomy tubes placed preoperatively at the time of staging laparoscopy to permit nutritional support during the course of neoadjuvant chemoradiation therapy, these tubes are maintained only in those patients who are nutritionally debilitated or at increased risk for this condition

after gastrectomy.



Adjuvant treatment:

Survival rates after resection for localized, node-negative gastric cancer approach 75% to 80% with surgery alone whereas survival rates drop to 10% to 30% with high local and distant recurrence rates. Recent studies using combined-modality therapy have shown significant improvement in survival rates in patients with gastric cancer.

Adjuvant Chemotherapy:

Large meta-analyses of adjuvant chemotherapy trials have suggested only minimal benefit and in particular just in subgroups of nodepositive or Asian patients. Most single agents have response rates in the 15% to 20% range, and although some small trials have shown a survival benefit, it has not been reproducible. Combination chemotherapy with agents such as 5-fluorouracil (5-FU), epirubicin, mitomycin, and methyl-CCNU have been associated with somewhat better response rates. Several meta-analyses of the randomized clinical trials of adjuvant chemotherapy have also been published, and even though some have suggested a small survival benefit, as well as the majority of individual studies, failed to show a significant survival advantage. In light of these nonconclusive results, routine adjuvant chemotherapy should be used only as part of a clinical trial.

Adjuvant Chemoradiotherapy:

The combination of chemotherapy and radiotherapy has been extensively studied in the treatment of many GI cancers, including gastric

cancer. Although early trials primarily using 5-FU and radiotherapy showed a small benefit, it was very difficult to draw definitive conclusions because of their small patient numbers, lack of standardization of surgical technique, and heterogeneous populations. The Gastrointestinal Cancer Intergroup Trial (INT-0116) randomized 556 eligible patients with stage IB to IV (M0) gastric cancer, who underwent margin-negative (R0) resection, to surgery alone or to surgery followed by bolus 5-FU/leucovorin (LV), followed by 45 Gy radiotherapy, followed by additional 5-FU/LV. Overall, 85% of patients were node positive and two thirds had T3 or T4 lesions. With more than 6 years of median follow-up, median disease-free survival was significantly improved in the adjuvant chemoradiotherapy group (30 versus 19 months, $P < .001$). Overall median survival was also significantly improved in the adjuvant chemoradiotherapy group (35 versus 28 months, $P = .01$). Given these results, postoperative chemoradiotherapy with this regimen has essentially become the standard of care for patients who have undergone curative resection for gastric cancer.

Adjuvant Intraperitoneal Therapy:

Because a significant proportion of postoperative recurrences in patients who undergo resection for gastric cancer occur in the peritoneal cavity, intraperitoneal (IP) therapy has been an attractive option. An initial randomized trial from Japan comparing IP mitomycin C with no postoperative therapy

showed a significant survival advantage of IP treatment. Subsequent studies, both retrospective and randomized, failed to show a survival benefit of IP mitomycin C, however, and actually suggested a significant increase in postoperative complications and mortality.

Similarly, continuous hyperthermic peritoneal perfusion (CHPP) has been used in patients with gastric cancer in both the adjuvant and palliative setting. This method relies on the synergistic effect of cytotoxic chemotherapy and hyperthermia. Several studies have reported on CHPP with mitomycin C after resection of gastric cancer.

Neoadjuvant Therapy:

Neoadjuvant or preoperative therapy has several theoretical advantages and has increasingly been used for the treatment of a variety of GI cancers. These advantages include improved patient tolerance, more effective delivery (increased oxygenation in the tumor bed), removal of treated tissue, early initiation of systemic therapy (in the case of preoperative chemotherapy), potential down-sizing of the primary tumor, ability to achieve better margins at resection, and evaluation of response to therapy, thereby adding to prognostic information and assisting in the planning of future therapy.

Neoadjuvant Radiotherapy:

Though seldom used without systemic chemotherapy, preoperative radiotherapy has shown promise in a few reports. A large randomized trial from China reported on 360 patients who underwent preoperative radiotherapy versus surgical resection alone. The radiotherapy group had a higher overall resection rate (89% versus 79%, $P < .01$) and 10-year survival rate (20% versus 13%, $P = .009$). Tumor down-sizing and nodal down-staging were also noted, and there was no increase in operative mortality with the use of preoperative radiotherapy. Patients with node-positive disease and T4 lesions had a significant survival advantage with the radiotherapy regimen, and again there was no increase in perioperative mortality or morbidity.

Neoadjuvant Chemotherapy :

Several phase II studies investigating systemic chemotherapy in the neoadjuvant setting have been reported and in general have suggested that preoperative chemotherapy can be given with acceptable toxicity and no increase in operative complications or mortality. Furthermore, overall survival in these trials was generally improved when compared with historical controls. In addition, it has been suggested in several trials that the response to chemotherapy was a significant predictor of survival.

More recently, preliminary results of the MAGIC trial from the United Kingdom were reported. In this randomized controlled trial, 503 patients with

adenocarcinoma of the stomach or lower esophagus were randomized to preoperative ECF, followed by surgery and postoperative ECF, versus surgery alone. No recommendation was given regarding the extent of lymphadenectomy because the results of the MRC and Dutch trials were unavailable at the start of this trial. The outcome was overall survival, progression-free survival, surgical resectability, and quality of life. Patients in both groups were well matched in age, gender, performance status, site, and pretreatment size of tumor. Operative complications, mortality, and length of hospital stay were similar in both groups. A higher proportion of patients in the chemotherapy group underwent curative resection (79% versus 69%, $P = .018$) and were noted to have significantly smaller tumors at surgery, as well as significantly lower T and N stages. Progression-free survival at 2 years was significantly improved in the ECF group (45% versus 30%, $P = .002$), but the improvement in overall survival did not quite reach statistical significance (48% versus 40%, $P = .063$; hazard ratio, 0.80; 95% confidence interval, 0.63 to 1.01). Although these results are preliminary and a longer follow-up period is needed, they strongly suggest a benefit of perioperative chemotherapy with the ECF regimen in patients with operable gastric cancer.

Neoadjuvant Chemoradiotherapy:

On the basis of the results of neoadjuvant chemoradiotherapy in the treatment of other cancers, including esophageal and rectal carcinoma,

multimodality regimens involving preoperative chemotherapy and radiotherapy are currently under study.

Because many of these trials are small and nonrandomized in nature, however, it is difficult to make definitive recommendations until larger prospective randomized trials are performed, and thus patients with resectable disease should receive preoperative chemoradiation only as part of a clinical trial.

Management of the advanced disease:

More than 50% of patients with gastric cancer have unresectable or metastatic disease at initial evaluation, and therefore appropriate use of palliative techniques is important.

Surgical palliation may include resection alone or in combination with endoscopic, percutaneous, or radiotherapeutic interventions. Other options for palliation include chemotherapy and radiotherapy. In the absence of prospective trials, the optimal choice for palliation is largely patient dependent.

Surgery for Palliation :

Because survival in patients with advanced gastric cancer is so short, any attempt at palliative resection should not only provide symptomatic relief but also be associated with minimal morbidity and mortality.

Although some of the studies data are retrospective, they do suggest that for select patients with symptomatic advanced gastric cancer, palliative resection may offer relief of symptoms for a majority of patients with acceptable morbidity and mortality. The treatment options may also largely depend on the extent of resection required for adequate palliation; for example, total gastrectomy with possible resection of adjacent organs is not usually indicated for palliation of unresectable disease.

Endoscopic Palliation:

In patients who are not good candidates for palliative resection but have symptoms of obstruction, endoscopic palliative techniques may be useful, including placement of metal expandable stents and laser recanalization. Although very limited prospective randomized data comparing endoscopic techniques and surgical bypass or resection are available, several studies suggest that both techniques are safe and can lead to some relief in many patients. Endoscopic stenting may result in similar short-term relief of obstruction as surgical bypass and is certainly a less invasive option.

Laser therapy can also be used as a complement to stenting and has been shown to provide short-term relief of obstruction in some patients.

Although none of these techniques would be expected to improve survival, they are good alternatives in patients who are not candidates for

palliative surgery but are suffering from signs of obstruction. After relief of obstruction, many of these patients can later receive palliative chemotherapy.

Generally patients with peritoneal disease, hepatic or nodal metastases, or other poor prognostic factors will probably benefit most from endoscopic palliation, including laser recanalization, dilatation, and stent placement. For patients with a better prognosis and excellent performance status, consideration can be given to surgical resection if it can be accomplished with minimal morbidity.

Palliative Chemotherapy:

Similar to the results of adjuvant therapy for resected gastric cancer, systemic chemotherapy for the advanced gastric cancer has been demonstrated to be beneficial. Several randomized trials, albeit small, have shown that patients receiving systemic chemotherapy have a longer median survival and better 1- and 2-year survival rates than with best supportive care alone. More recently, combination chemotherapy with agents such as cisplatin, paclitaxel, and irinotecan have shown similar response rates and median survival times in several phase II studies. Certainly, multiagent chemotherapy should be offered to all patients with advanced disease who have reasonable performance status.

Palliative Radiotherapy:

Experience with radiotherapy in patients with advanced gastric cancer is much more limited. Although its use seems to be fairly effective in controlling symptoms such as bleeding and pain, most patients have diffuse metastatic disease, and the use of radiotherapy alone would not be expected to provide much increase in overall survival.

MATERIALS AND METHODS

Our hospital is a referral centre for gastro intestinal disease with attached institute of surgical and medical gastroenterology.

Cases for this study has been selected from 2012 to 2014 from the following departments:

1. Dept. of General Surgery[all 7 units].
2. Dept of Surgical gastroenterology.
3. Dept of Medical oncology.

Total population:

50 cases.

Study design:

Retrospective cum prospective study

Patient selection criteria:

All patients with operable gastric adenocarcinoma and not included in the exclusion criteria.

Exclusion criteria:

Patients with cardiovascular diseases, diabetes, acute/chronic inflammatory diseases, previous malignancy, or previous thromboembolic events and inoperable cases of gastric adenocarcinoma.

All the patients in this study were given information of the study and explained its merits and demerits and obtained consent from them.

The protocol for evaluation of carcinoma stomach in our institution as follows:

a. All the patients presenting to the outpatient department with the complaints of vomiting/ epigastric pain/ dysphagia / melena/ haemetemesis/ lose of weight/ lose of appetite/ ball rolling movements are subjected to thorough history and clinical examination
b. All patients presenting with abdominal pain and dyspepsia above the age of 40 years is also subjected to thorough history and clinical examination and the same subjected to endoscopic examination
c. Those who are less than 40yrs with abdominal pain and dyspepsia , if not resolved with conservative management are subjected to endoscopy.
d. Those who are diagnosed to have endoscopic findings suggestive malignancy are admitted in the ward.

e. During endoscopy, we employ a technique of multiple biopsies from all sides of the lesion. A maximum of six to eight bits of tissue has been taken and sent to pathological department for histopathological examination.

f. A Complete blood count , Platelet count , Renal function test , Liver function test, and coagulation profile are obtained for all the patient along with plain chest roentgenogram and ECG.

g. With the above investigations pre operative assessment will be obtained for the patient after correcting in presence of any abnormalities.

h. Ultrasonogram of the abdomen is done as a screening procedure to look for ascites, liver metastasis, other distant metastasis if possible.

i. If ultrasonogram shows no signs of metastasis, contrast enhanced computed tomography[CECT] of the abdomen is done to stage the disease.

j. If CECT abdomen also rules out any metastasis, then a diagnostic laproscopy ander general anaesthesia will be planned and proceded to look for any radiologically undetectable metastasis in the liver, peritoneum, pelvic organs and the adjacent spread of tumor beyond the serosa to the nearby organs the pancreas, left lobe of liver, spleen and duodenum.

k. If all the above investigations have been ruled out the presence of extra serosal spread and distant metastasis then the patient and his/her family members are informed about the nature of the disease, perioperative morbidity and mortality, post operative treatment in form of chemotherapy to control systemic micrometastasis.

l. In surgery, a curative resection in the form of subtotal gastrectomy / total gastrectomy according to the location of the tumor with D2 lymphadenectomy is done.

m. And the specimen is sent to the pathological department for histopathological examination to look for grade of the tumor, stage of the tumor, margin status, and lymphnode status.

n. If the preoperative investigations shows distant metastasis or the tumor is inoperable peroperatively, patient will be referred to the oncology department for palliative chemotherapy provided there is no features of gastrointestinal tract obstruction.

o. In case of obstruction a feeding jejunostomy/ a palliative resection with anastamosis of the remaining bowel will be done.

p. All of those patients who underwent curative resection will be subjected for adjuvant chemotherapy and followed up at regular intervals for recurrence.

RESULTS:

A total number of 50 operable cases of gastric adenocarcinoma were subjected for this study. Their coagulation profile specifically the prothrombin time and the nodal positivity/negativity in resected specimen has been studied.

In our study the age distribution varies from 25 years to 80 years. But the increased incidence has been observed among the age group of 41-50years of 38%.

The mean age of presentation is calculated to be around 54. Even though incidence increases with age, the cases around the age group of 25yrs has been reported in our study.

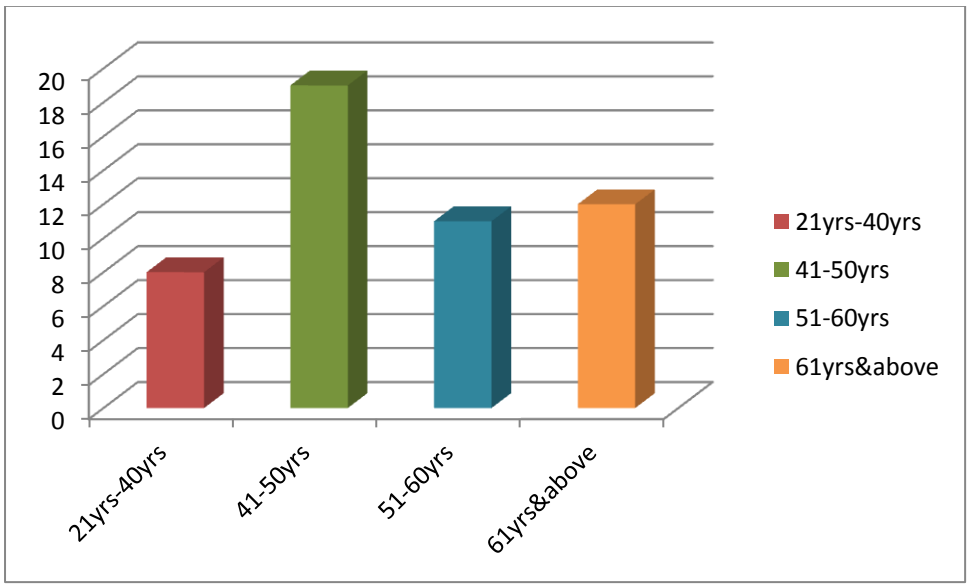


TABLE 1- AGE DISTRIBUTION.

TABLE.2-COMPARISON BETWEEN AGE GROUP & NODAL METASTASIS

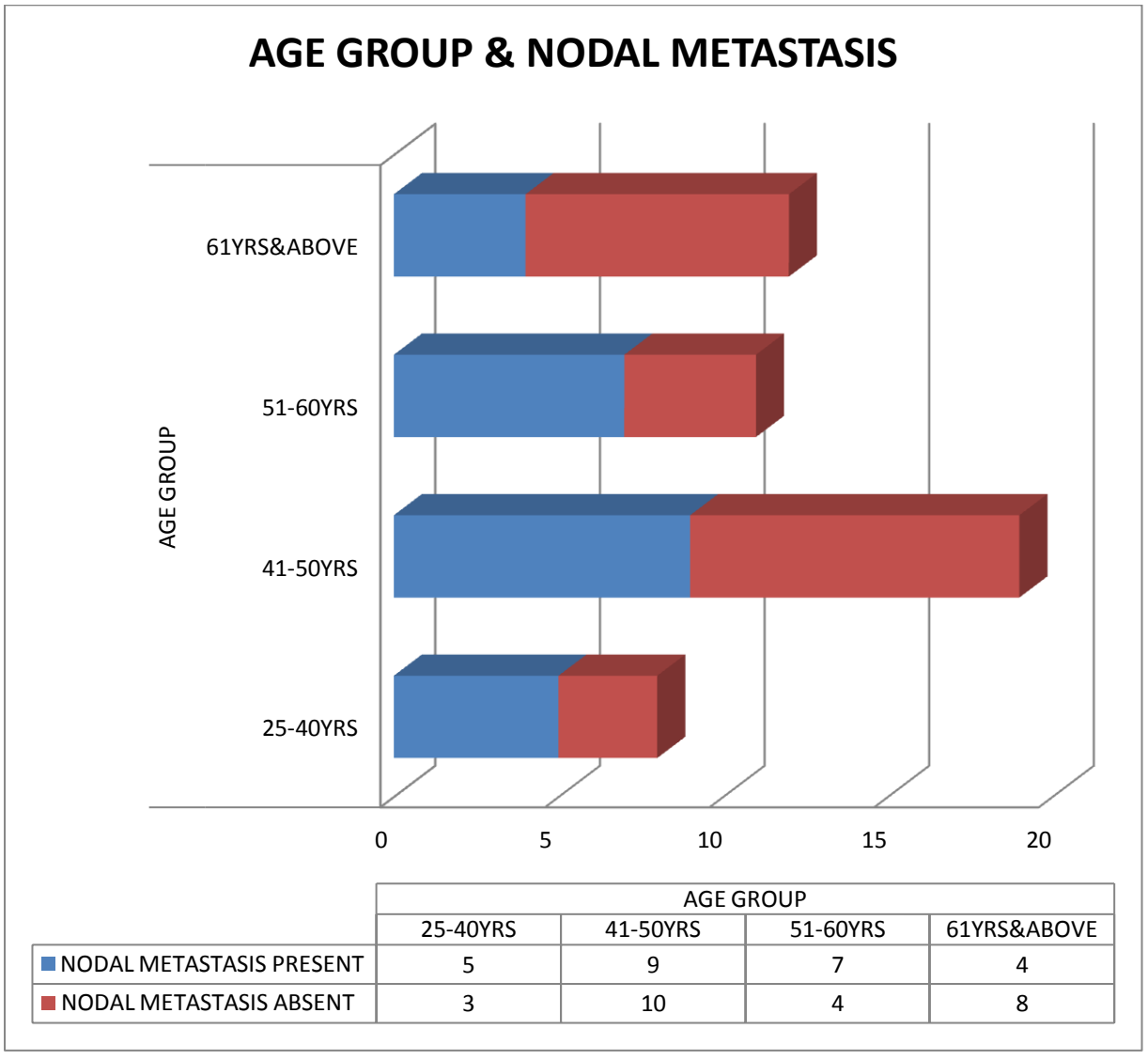
AGE GROUP		NODAL METASTASIS		
		PRESENT	ABSENT	TOTAL
25yrs-40yrs	Count	5	3	8
	% within age group	62.5%	37.5%	100.0%
	% within nodal metastasis	20.0%	12.0%	16.0%
41yrs-50yrs	Count	9	10	19
	% within age group	47.4%	52.6%	100.0%
	% within nodal metastasis	36.0%	40.0%	38.0%
51yrs-60yrs	Count	7	4	11
	% within age group	63.6%	36.4%	100.0%
	% within nodal metastasis	28.0%	16.0%	22.0%
61yrs& above	Count	4	8	12
	% within age group	33.3%	66.7%	100.0%
	% within nodal metastasis	16.0%	32.0%	24.0%
TOTAL	Count	25	25	50
	% within age group	50.0%	50.0%	100.0%
	% within nodal metastasis	100.0%	100.0%	100.0%

IN the Table.2, age groups of the patients selected in our study has been compared with the incidence of nodal metastasis in the respective groups.

Statistical analysis of this comparison has been done by using the PEARSON CHI SQUARE test

The p value obtained for this comparison is statistically insignificant.

Table.3- Age group & Nodal metastasis comparison



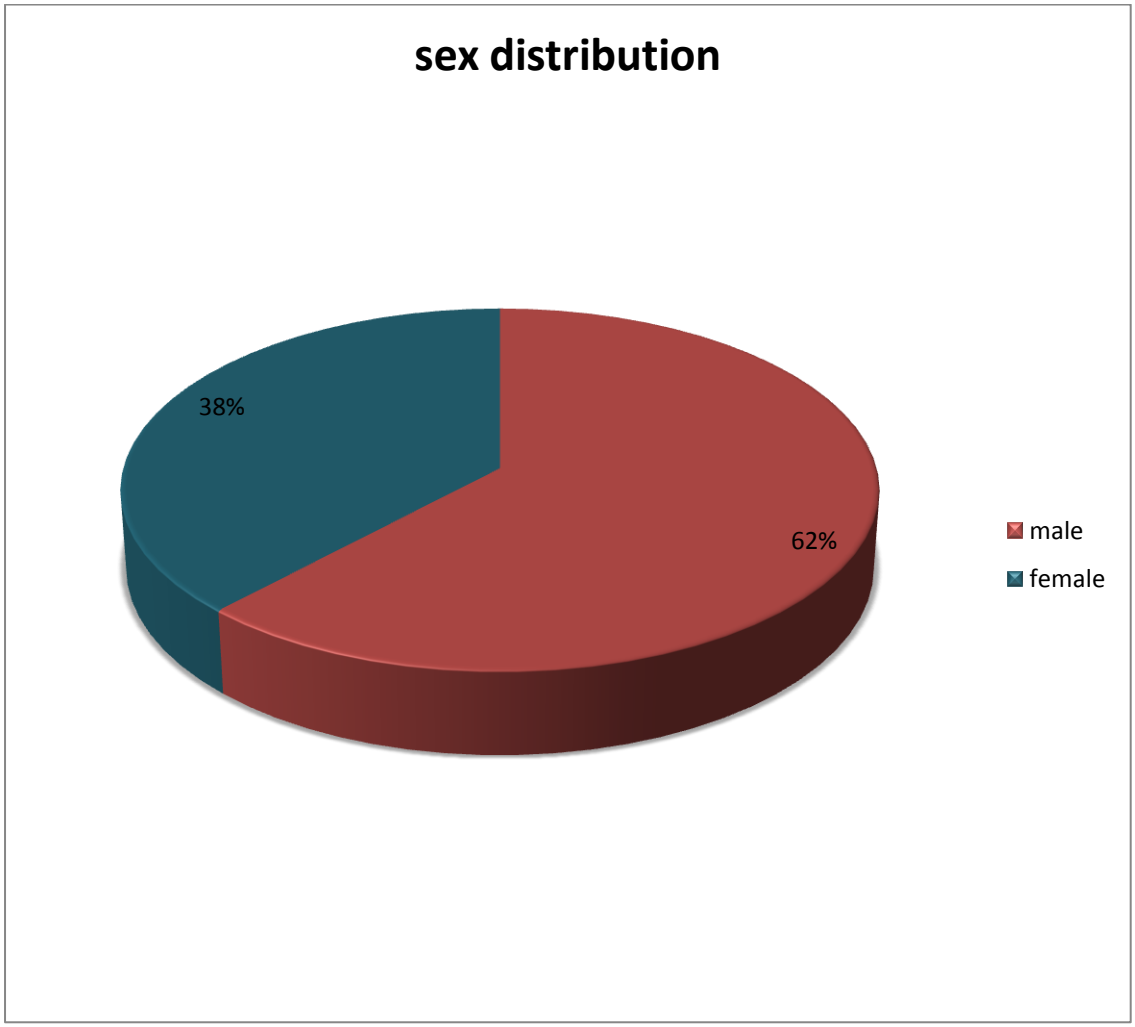
	AGE GROUP			
	25-40YRS	41-50YRS	51-60YRS	61YRS&ABOVE
NODAL METASTASIS PRESENT	5	9	7	4
NODAL METASTASIS ABSENT	3	10	4	8

The CHI SQUARE value was 2.704 & the p value was 0.440.

The sex prevalence among the study group includes 19 females and 31 males, thus the incidence of 38% and 62% respectively.

So this shows the prevalence of the gastric adenocarcinoma more among the males than females.

Table.4-Sex distribution



In table 5 the sex groups both male and female has been compared with the presence of nodal metastasis in their according groups

The statistical analysis of this comparison has done by using PEARSON CHI SQUARE TEST

The p value obtained is statistically insignificant.

	Sex	nodal metastasis		
		0	1	Total
F	Count	11	8	19
	% within sex	57.9%	42.1%	100.0%
	% within nodal metastasis	44.0%	32.0%	38.0%
M	Count	14	17	31
	% within sex	45.2%	54.8%	100.0%
	% within nodal metastasis	56.0%	68.0%	62.0%
Total	Count	25	25	50
	% within sex	50.0%	50.0%	100.0%
	% within nodal metastasis	100.0%	100.0%	100.0%

Table.5 Comparison between sex and nodal metastasis.

Chi-square value was 0.764 and p value was 0.382

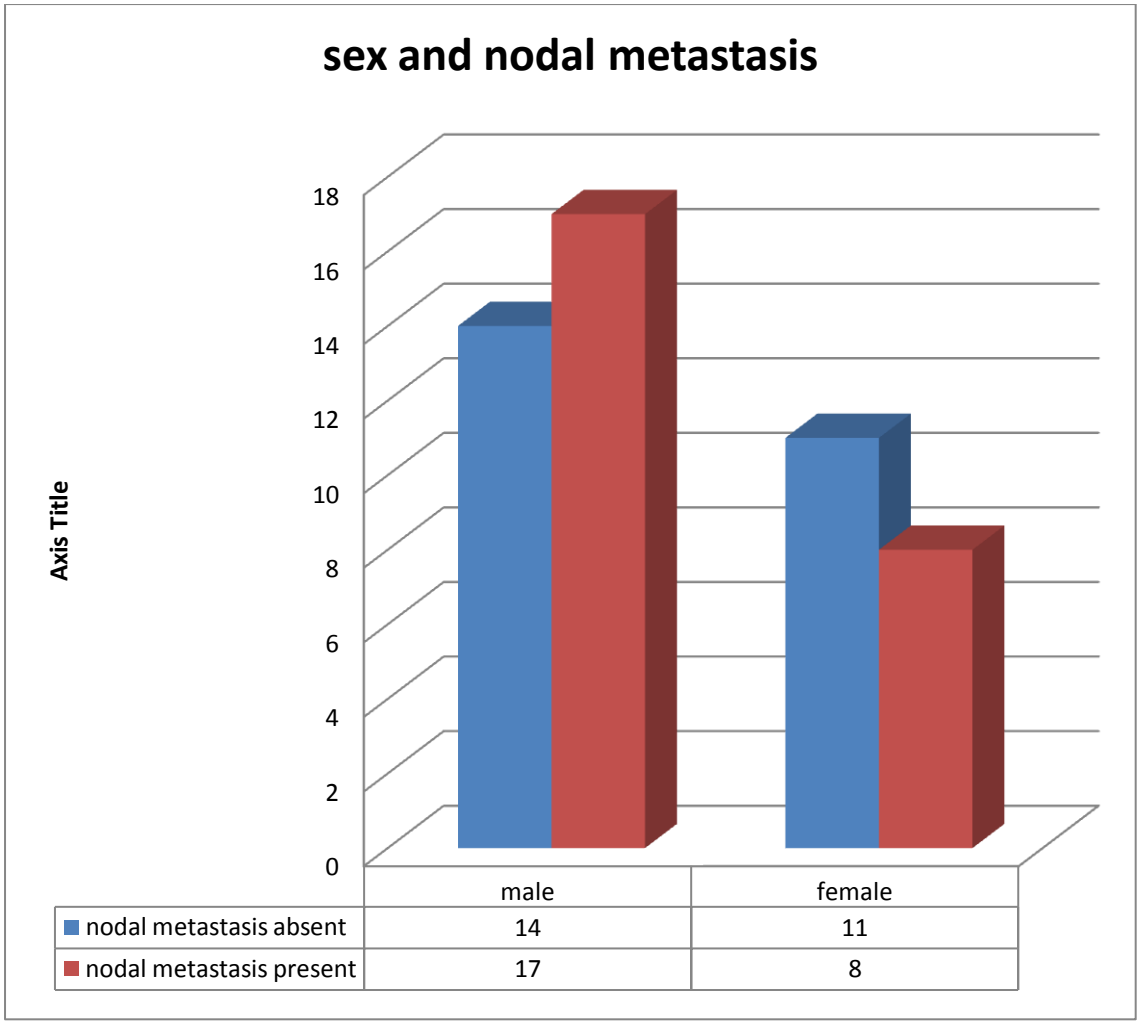


Table.6 sex and nodal metastasis comparison.

Based on the location of the tumor in the stomach the incidence of the tumor has been studied and as follows:

Fundus of stomach-4% cases, Fundus & Body of stomach-6% cases, Body of stomach-20% cases, Antrum-30% cases, Antropyloric region-40% cases.

The antropyloric region contributes the most indicating that the distal cancers are more common and also presenting at the earlier stage according to this study.

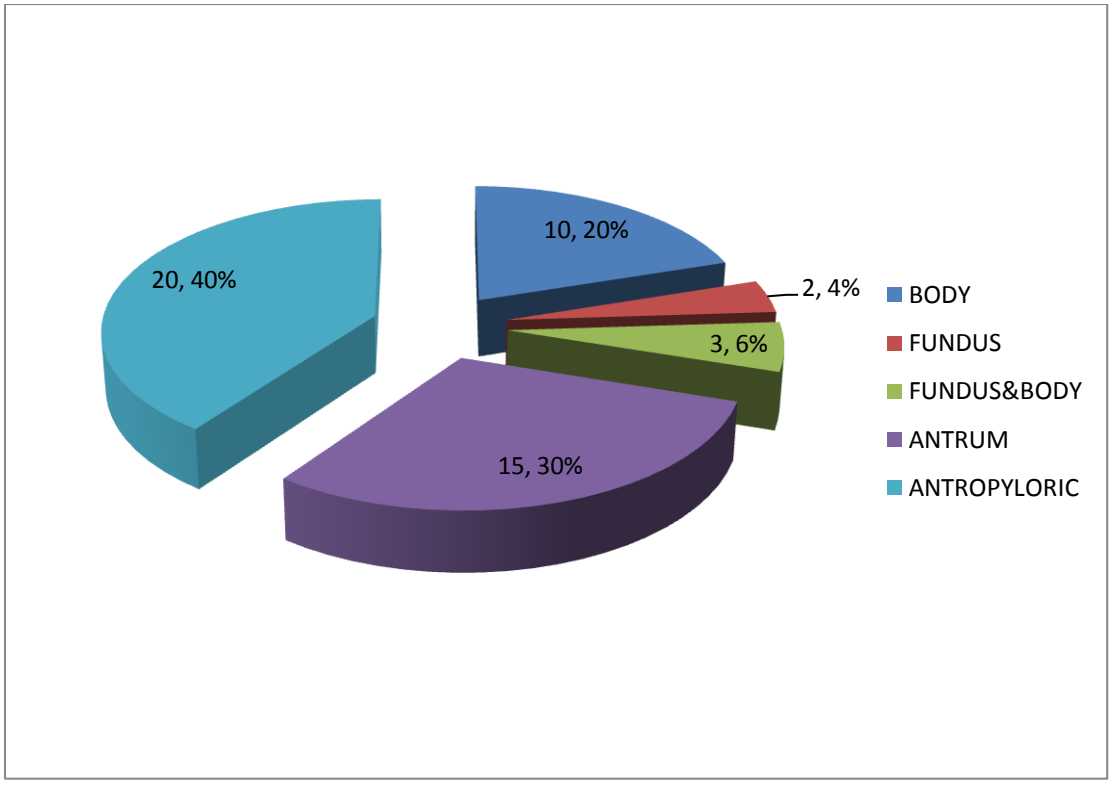


Table.7 Location of tumor and incidence.

The location of the tumor and prevalance of nodal metastasis has been compared to know the specific predisposition among any groups.

This comparison has been done by using PEARSON CHI SQUARE test

The p value obtained is statistically insignificant.

			nodal metastasis		
			0	1	Total
LOCATION OF THE TUMOR	ANTRUM	Count	10	5	15
		% within LOCATION OF THE TUMOR	66.7%	33.3%	100.0%
		% within nodal metastasis	40.0%	20.0%	30.0%
		% of Total	20.0%	10.0%	30.0%
	ANTRO-PYLORIC	Count	9	11	20
		% within LOCATION OF THE TUMOR	45.0%	55.0%	100.0%
		% within nodal metastasis	36.0%	44.0%	40.0%
		% of Total	18.0%	22.0%	40.0%
	BODY OF STOMACH	Count	5	5	10
		% within LOCATION OF THE TUMOR	50.0%	50.0%	100.0%
		% within nodal metastasis	20.0%	20.0%	20.0%
		% of Total	10.0%	10.0%	20.0%
	FUNDUS	Count	1	1	2
		% within LOCATION OF THE TUMOR	50.0%	50.0%	100.0%
		% within nodal metastasis	4.0%	4.0%	4.0%
		% of Total	2.0%	2.0%	4.0%
	FUNDUS &	Count	0	3	3

	BODY	% within LOCATION OF THE TUMOR	.0%	100.0%	100.0%
		% within nodal metastasis	.0%	12.0%	6.0%
		% of Total	.0%	6.0%	6.0%
	Total	Count	25	25	50
		% within LOCATION OF THE TUMOR	50.0%	50.0%	100.0%
		% within nodal metastasis	100.0%	100.0%	100.0%
		% of Total	50.0%	50.0%	100.0%

Table 8.Location of tumor &nodal metastasis comparison

The CHI SQUARE value is 4.867 and the p value is 0.3

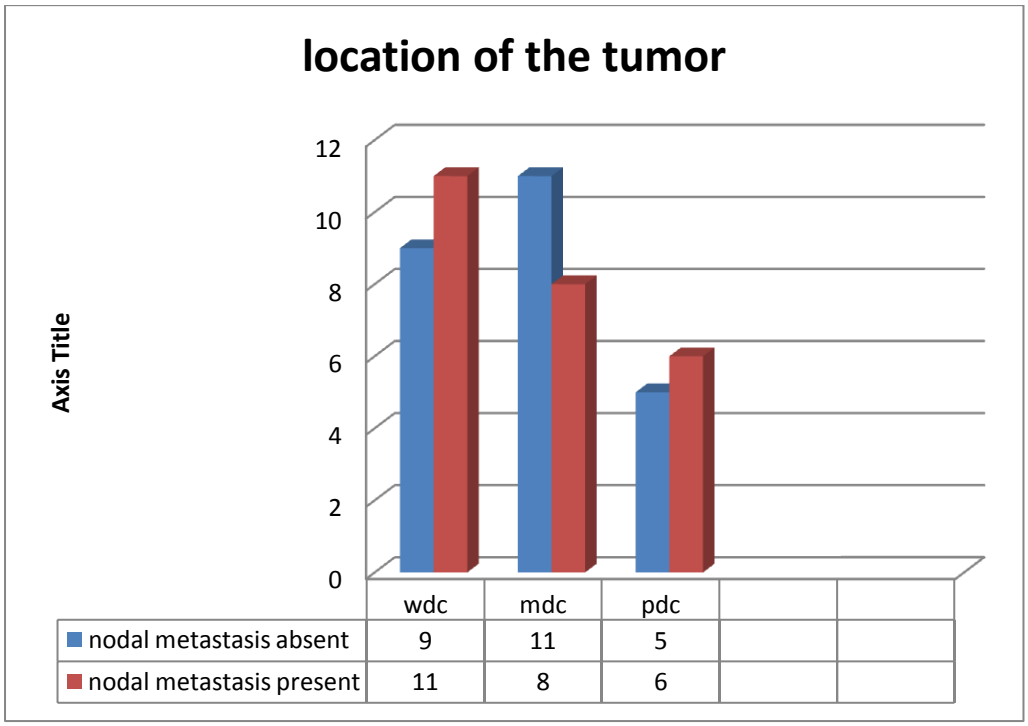


Table.9 location of tumor & nodal metastasis comparison.

The histopathological examination of the specimen studied and reported

According to lauren's classification, the histology of adenocarcinoma of stomach has been divided into two types:

1.Intestinal type.

2.Diffuse type.

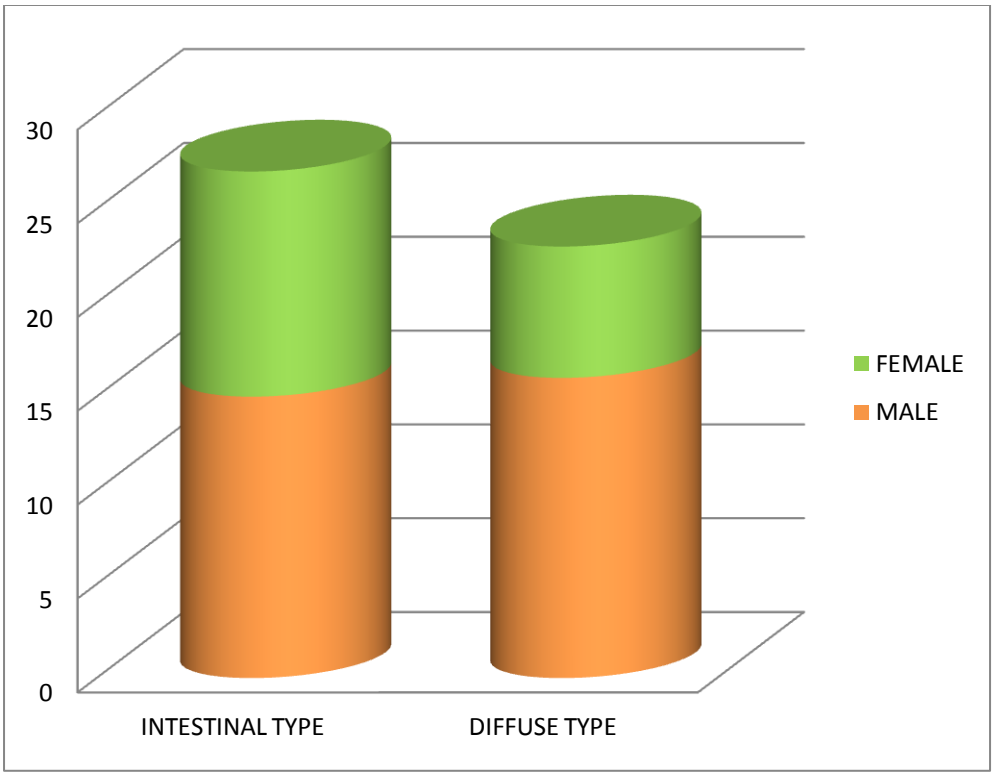


Table.10. Type of carcinoma

The histological type of carcinomas also compared with the incidence of nodal metastasis in their groups.

The study used here is the PEARSON CHI SQUARE test

The p value is statistically insignificant.

			nodal metastasis		
			0	1	Total
carcinoma type	Diffuse type	Count	12	11	23
		% within carcinoma type	52.2%	47.8%	100.0%
		% within nodal metastasis	48.0%	44.0%	46.0%
		% of Total	24.0%	22.0%	46.0%
	Intestinal type	Count	13	14	27
		% within carcinoma type	48.1%	51.9%	100.0%
		% within nodal metastasis	52.0%	56.0%	54.0%
		% of Total	26.0%	28.0%	54.0%
	Total	Count	25	25	50
		% within carcinoma type	50.0%	50.0%	100.0%
		% within nodal metastasis	100.0%	100.0%	100.0%
		% of Total	50.0%	50.0%	100.0%

Table.11 Carcinoma type & nodal metastasis.

The CHI SQUARE test value is 0.081

The p value is 0.777.

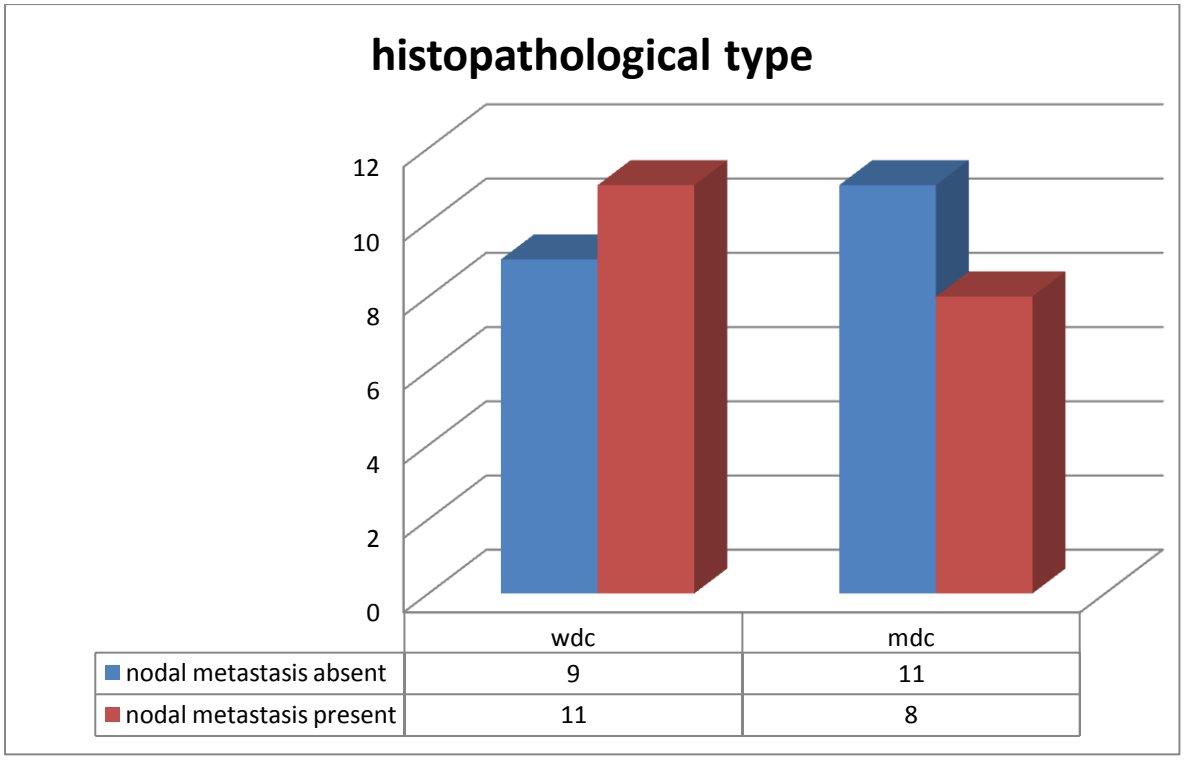


Table .12. Carcinoma type and nodal metastasis comparison.

The differentiation of the carcinomas studied from the post operative specimen and they are divided as:

1. Well differentiated carcinoma

2. Moderately differentiated carcinoma.

3. Poorly differentiated carcinoma.

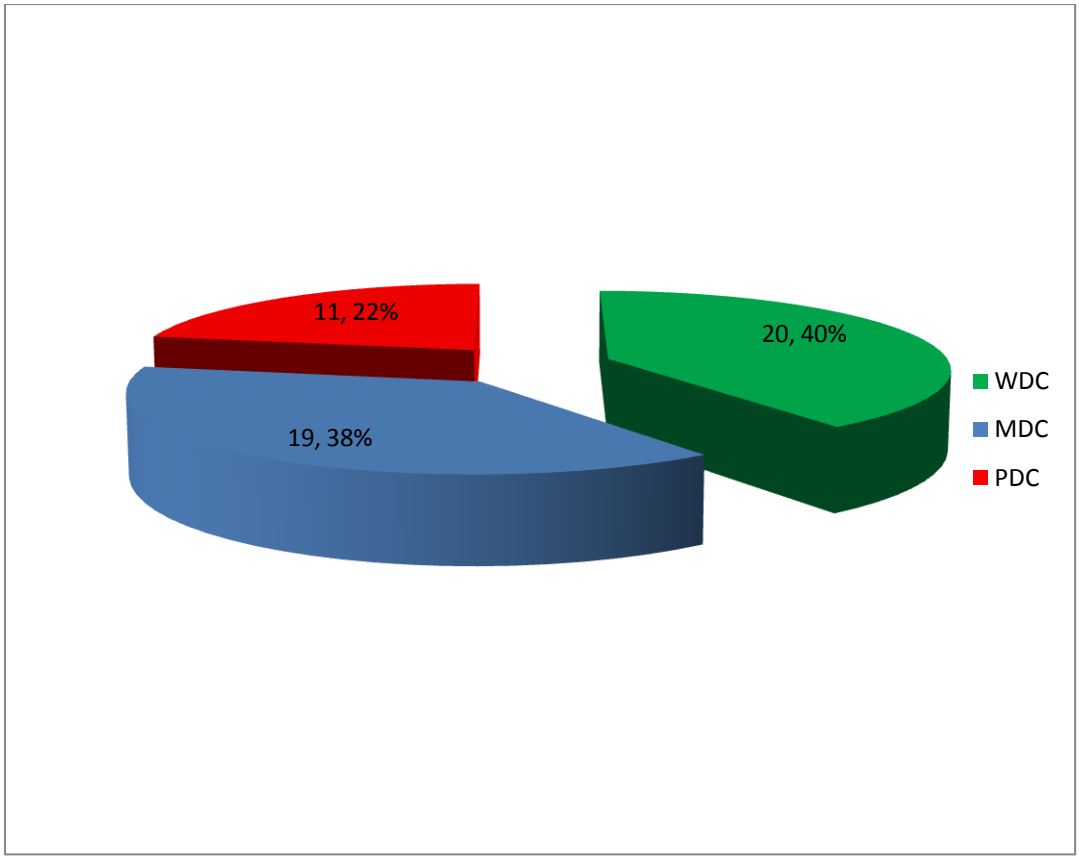


Table.13. Differentiation of carcinoma types and their distribution.

The comparative study done among these groups to found out that association between differentiation of carcinoma and nodal metastasis by using the PEARSON CHI SQUARE test

The p value obtained is statistically insignificant.

			nodal metastasis		
			0	1	Total
DIFFERENTIATION	MDC	Count	11	8	19
		% within DIFFERENTIATION	57.9%	42.1%	100.0%
		% within nodal metastasis	44.0%	32.0%	38.0%
		% of Total	22.0%	16.0%	38.0%
	PDC	Count	5	6	11
		% within DIFFERENTIATION	45.5%	54.5%	100.0%
		% within nodal metastasis	20.0%	24.0%	22.0%
		% of Total	10.0%	12.0%	22.0%
	WDC	Count	9	11	20
		% within DIFFERENTIATION	45.0%	55.0%	100.0%
		% within nodal metastasis	36.0%	44.0%	40.0%
		% of Total	18.0%	22.0%	40.0%
	Total	Count	25	25	50
		% within DIFFERENTIATION	50.0%	50.0%	100.0%
		% within nodal metastasis	100.0%	100.0%	100.0%
		% of Total	50.0%	50.0%	100.0%

Table.14. Carcinoma differentiation & nodal metastasis comparison.

The CHI SQUARE value is 0.765.

The p value is 0.682.

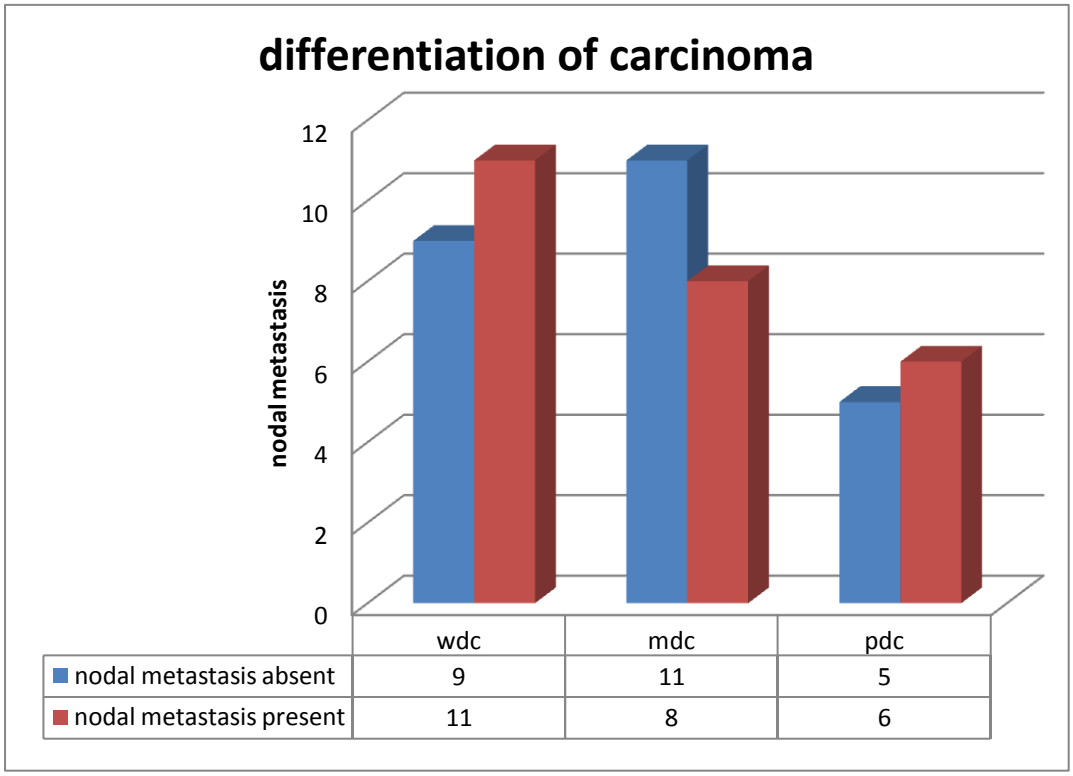


Table.15.Carcinoma differentiation & nodal metastasis comparison.

The prothrombin time taken preoperatively for these patients are compared with the nodal metastasis. The normal prothrombin time [INR] is taken as 0.85-1.15.

The comparison study is used is PEARSON CHI SQUARE TEST

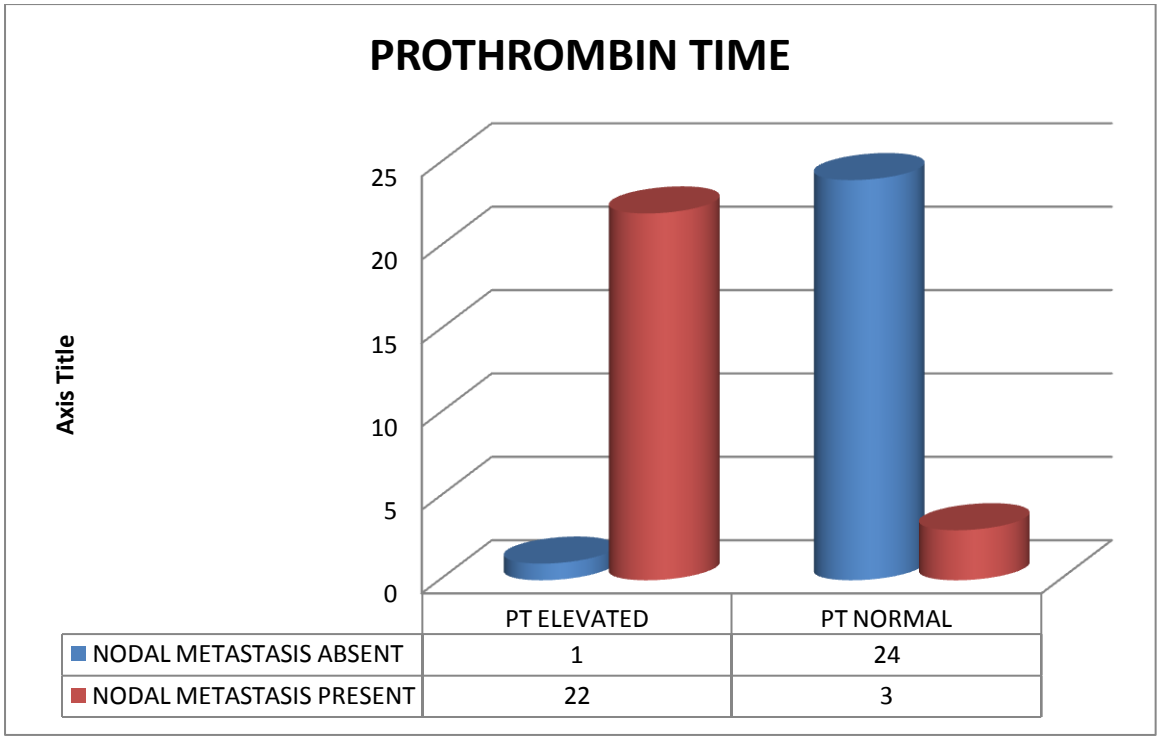
The p value obtained is statistically found to be significant.

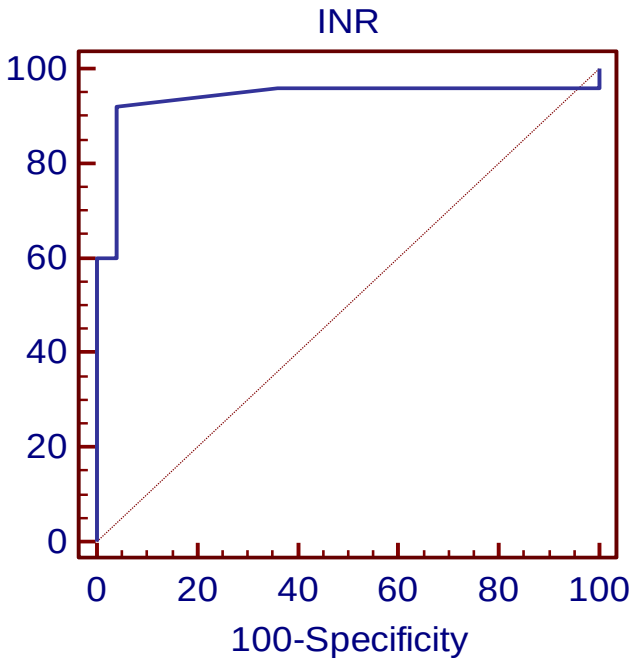
			nodal metastasis		
			0	1	Total
prothrombin time	0	Count	24	3	27
		% within prothrombin time	88.9%	11.1%	100.0%
		% within nodal metastasis	96%	12%	54.0%
		% of Total	48.0%	6.0%	54.0%
	1	Count	1	22	23
		% within prothrombin time	4.3%	95.7%	100.0%
		% within nodal metastasis	4%	88%	46.0%
		% of Total	2%	44%	46.0%
	Total	Count	25	25	50
		% within prothrombin time	50.0%	50.0%	100.0%
		% within nodal metastasis	100.0%	100.0%	100.0%
		% of Total	50.0%	50.0%	100.0%

Table.16. prothrombin time & nodal metastasis comparison.

The CHI SQUARE value is 35.507.

The p value is <0.0001.





The AUC of this ROC curve is 0.939200.the standard error is 0.0425. the odds ratio calculated suggests 176 times risk of nodal metastasis in the presence of prothrombin time elevation.

Discussion:

Recent study by D.M.RODER on gastric cancer epidemiology conducted globally have shown that the incidence of gastric cancer has been reduced, with a male preponderance of about 2.2 times compared to the females and also the increased occurrence of intestinal type than diffuse type. In our study this has been proved that male preponderance mdue to smoking&alcoholism. Also the intestinal type is on a slightly higher hand in our study.

But the same study have shown that the incidence of proximal gastric cancers are more common whereas in our study the distal gastric cancers are more common than the proximal ones.

Many studies have shown that there was a disregulation of the coagulation factors in the blood especially in patients with solid tumors of any origin and their disregulation corresponds according to the progression of the disease.

1.Hyuk-chan kwon et al. studied about the correlation between the plasma levels of Prothrombin time, D-dimer, Prothrombin fragment with the clinical stage and nodal metastasis in gastric cancer cases, they reported that the prothrombin time & prothrombin frgment were correlated with the staging and lymph node metastasis of gastric cancer patients whereas the d-dimer, activated partial thromboplastin time and fibrin degradation products correlation were not

statistically significant.The p value for prothrombin time was 0.010 and for prothrombin fragment it is 0.023.

2. Hiroharu yamashita et al., studied the usefulness of hyperfibrogenemia in predicting the lymphatic metastasis in gastric cancer patients. He compared preoperative C reactive protein level, carcinoembryonic antigen and plasma fibrinogen levels with the nodal metastasis in his study and concluded that the increased plasma fibrinogen level was

Independently associated with lymphatic metastasis of gastric cancer

3.Fang-xuan li et al., conducted a study to know the relationship of platelet count and the progression of gastric cancer. He concluded that the thrombocytosis and the progression of gastric cancer are correlated.

4.L.M.rohsig et al., studied the correlation between the levels of von willebrand factor in the plasma and the disease progression in breast cancer patients. He concluded that there is a significant rise in the plasma levels of von willebrand factor in the advanced cases than earlier breast cancer patients indicating the correlation between them.

5.Hiroharu yamashita et al., studied about the influence of tissue factor on the disease progression & lymphatic metastasis in cases of gastric cancer. He concluded that the the tissue factor expression has a

positive correlation with the tumor progression and nodal metastasis in intestinal type of gastric cancer with a p value of 0.0001.

6. Masataka ikeda MD et al., studied around 350 patients of gastric cancer and their hemoglobin,platelet levels in blood. From his study he concluded that the thrombocytosis has been found to be a independent

Indicator of poor prognosis in these patients.

7.Yoshihisa tezuka et al.,studied about 106 patients with esophageal squamous cell carcinoma and the staining for thrombomodulin of the resected specimens, he found out that the decrease in the staining of this anticoagulant in the metastatic nodes thereby indicating the thrombomodulin downregulation during tumor progression and metastasis

8.Long liu et al., studied about the relation between the D dimer levels and the peritoneal dissemination, nodal metastasis, depth of invasion in gastric cancer patients. He concluded the study stating that the plasma D dimer levels had positive correlation with peritoneal dissemination and nodal metastasis of the patients thereby helps in predicting the overall survival of the patients.

9. Kimberly Blackwell et al., investigated the relationship between plasma D dimer levels and the extent tumor involvement in operable cases of breast cancer. He found out that the plasma D dimer levels

were correlated well with the axillary lymph nodal metastasis with a p value of 0.0053.

10.Marek Z. Wojtukiewicz et al., studied the expression of various coagulation factors such as tissue factor, prothrombin fragment, fibrin in the cases of breast cancer in the breast tissue and the nodal tissue. He found the overexpression of these factors in the tumor tissue and nodal tissue suggesting their role in tumor progression and metastasis.

11.D.Ferrigno et al.,assessed the significance of coagulation factors in relation to the prognosis of lung cancer anf he founded that the coagulation factors especially the D dimer, prothrombin time, and others were significant in predicting the survival of lung cancer patients.

In our study,50 cases of operable gastric cancer have been chosen.

Of which 25 cases are node positive & rest of them were node negative as per the post operative biopsy reports.

Among these two groups about six factors has been compared. They are as follows:

1. AGE.
2. SEX.
3. HISTOLOGICAL TYPE OF CARCINOMA.

4. LOCATION OF THE PRIMARY TUMOR.

5. DIFFERENTIATION OF THE CARCINOMA

6. PROTHROMBIN TIME

Of the above factors, we founded that there was a

Male preponderance in the study groups,

Increased incidence among the fourth decade of life,

Increased occurrence of the distal gastric cancers among this group,

And then the most important thing the nodal metastasis which decreases the overall survival if present is found to be correlated well with the elevation in prothrombin time

It has been found out that none of the aforementioned factors except the prothrombin time elevation can be helpful in the prediction of the nodal metastasis, thereby the disease progression and overall survival in gastric cancer patients.

Conclusion:

From, this study we have concluded that there exists disregulation of prothrombin time among the gastric cancer patients and also the prothrombin time elevation has a positive correlation with lymph node metastasis and thereby the tumor progression among the operable cases of gastric cancers.

As the curative resection being the mainstay of management of gastric adenocarcinoma, addressing the possible mode and site of metastasis prior to surgery is mandatory for the surgeons so as to plan the appropriate mode of management.

Many of the studies have been suggesting the role of coagulation factors in the tumor metastasis either by hematogenous/lymphatic route by supporting the tumor emboli evading the innate defenses against this activity.

We suggest that this study could be an adjunct to this hypothesis there by helping in the formulation of new target therapy against the metastasis of the tumor emboli by adding the anticoagulants with the adjunct therapy thereby helps in increased resection of the tumors than going for palliative therapy due to metastasis.

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